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Editorial

From Principle to Practice

'Both States of export and States of import should protect human health and the environment against potential harm by exchanging information on chemicals in international trade.'

The above general principle was unanimously adopted by Governments in 1987 when endorsing the London Guidelines for the Exchange of Information on Chemicals in International Trade. The Guidelines further stipulate that States should facilitate the exchange of scientific information (including toxicological and safety data) and technical, economic and legal information concerning the management of chemicals, particularly through designated national governmental authorities and through intergovernmental organizations as appropriate.

The regular reader of the IRPTC Bulletin *probably recalls that IRPTC in the first issue, dated December 1977, reported on a similar discussion by the UNEP Governing Council, when approving the establishment of IRPTC as a novel activity in the United Nations system devoted to information exchange on chemicals.*

IRPTC was considered to be an essential tool in optimizing the use of chemicals for human well-being and at the same time providing a global early warning system of undesirable environmental side effects. It was expected to facilitate access on a global basis to scientific and legal data concerning potentially toxic and other environmentally significant chemical substances and to encourage international cooperation in determining the impact of chemicals on man and the environment. IRPTC would also encourage a more open relationship between industry and regulatory authorities, in both industrialized and developing countries, in order to make relevant data more readily available.

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Since then, IRPTC has built its global network for information exchange and has intensified the flow of scientific, technical and regulatory information on chemicals. It has developed central data files on many chemicals of international significance which are now being increasingly used for hazard assessment and risk evaluation at both national and international levels. Training is being provided to familiarize National Correspondents and others with the use of the Register. The establishment of compatible national registers is being promoted and data dissemination will increasingly take place through interactive networking, on-line access to the central files and by other means. Very shortly IRPTC hopes to provide a well-tested, user-friendly system for use of IRPTC data on personal computers which at the same time can be used for contributing data to the central files of the Register.

'Our Common Future', the report of the World Commission on Environment and Development published in 1987, refers to IRPTC as a notable example of an international information exchange network and a data base on chemicals which should be strengthened by Governments. In the same year, the General Assembly of the United Nations in its Environmental Perspective to the Year 2000 and Beyond recommended that 'IRPTC should maintain and improve its assistance to Governments in assessing whether producing, marketing, distributing or disposing of any industrial substances, including chemicals and wastes, are potentially damaging to health and the environment'.

The unique character of the IRPTC concept, a data-bank connected to an information exchange network, enables the Register to assist Governments in their efforts to improve chemical safety at the national level. On the other hand, it also provides an excellent opportunity for Governments and others to assist the Register in its attempts to intensify and harmonize information flows on chemicals of international significance.

Of course, IRPTC is not the only actor— it works closely with the International Programme on Chemical Safety, and is actively involved in, for example, relevant programmes of EEC, OECD and CMEA related to chemical safety.

The importance of such cooperation among countries and with other international organizations was stressed recently during the Meeting on the Protection of the Environment of the Conference on Security and Cooperation in Europe which took place in Sofia (November 1989).

It seems that we are moving from adopting principles to establishing practices. Governments, industry and international organizations are all recognizing the need for strengthening international exchange of information and for cooperation on chemicals. IRPTC has developed the tool to provide for such information exchange in a harmonized adaptable manner, based on sound scientific and technical principles. It has been recognized as a suitable instrument in the hands of experts to participate in such information exchange. It should now be introduced and used in national and international programmes aimed at strengthening international cooperation in managing hazardous chemicals. Who could be interested in a Babylonian confusion of tongues?

OECD Member Countries agree to expand their efforts to share the burden of work on chemical safety

OECD Member Countries agreed today to embark on a major new effort to jointly carry out a Systematic Investigation of the potential health and environmental effects of chemicals produced in the largest quantities worldwide. Member countries have selected 150 of these chemicals as the first subjects of this investigation. Each of these chemicals is made in quantities exceeding 1,000 tonnes per year in at least one OECD country. High production chemicals are of particular interest since they are the ones to which humans and the environment are most likely to be exposed.

The 150 chemicals were chosen as priorities from among nearly 1,500 produced in high volumes within OECD Member Countries. Experts from 15 OECD Member Countries, working under the joint chairmanship of the Federal Republic of Germany and Sweden in close collaboration with two organizations of the United Nations (the International Programme on Chemical Safety (IPCS) and the International Register of Potentially Toxic Chemicals (IRPTC), have analysed their data availability.

A major finding is that for almost 150 of the total number of high production volume chemicals there seems to be a lack of basic data needed for identifying potential risk to health or the environment....

Further work remains to complete and agree on the protocols for developing the basic data (the Screening Information Data Set (SIDS)) to be generated for the 150 chemicals. Depending on the amount of testing needed to complete the SIDS, the cost per chemical could be as high as US$ 200,000.

It was further agreed that this work would be carried out in collaboration with the Commission of the European Communities, the United Nations International Programme on Chemical Safety and the International Register of Potentially Toxic Chemicals....

This agreement is a milestone in international work on chemicals: the first major collective information gathering, testing and screening of a large group of industrial chemicals. The goal of this new project is to complete, by the end of 1993, sufficient work on each of these 150 important chemicals in order to screen their potential to cause adverse health or environmental effects. That information will, through a variety of mechanisms such as the evaluations of the IPCS and the data profiles of IRPTC, be made available to the users of chemicals worldwide.

OECD Press release, 9 November 1989.

I. IRPTC and UNEP Activities

National Correspondents

The National Correspondents play an important role in all IRPTC's activities. They possess, and are able to call upon, expertise and experience in the fields of toxicology, public health, occupational health, agriculture, industrial and environmental sciences. As environment is an interdisciplinary subject, environmental protection services in most countries are shared among a number of authoritative bodies. Therefore, National Correspondents need to have close links with all these bodies and establish direct contact with other institutions and individuals responsible for the control of chemicals in their countries. In addition they assist IRPTC by obtaining information on the following: relevant national legislation and regulations on control of chemical hazards; the existence of national criteria documents, reviews, and reports on chemicals; report on accidents and incidents resulting from loss of chemicals into the environment; and the existence of data banks and other information systems relevant to IRPTC's requirements. They also assist in the operation of the Query-Response Service and are responsible for promoting and distributing of IRPTC publications to interested individuals, institutions, and industries in their respective countries.

In addition, several National Correspondents, have been nominated by their respective Governments as Designated National Authorities for the implementation of the London Guidelines for the Exchange of Information on Chemicals in International Trade (see this issue, page 4). They have sent notifications of control actions on many chemicals taken in their countries which were processed and disseminated by IRPTC to all other Designated National Authorities.

During 1988-89, IRPTC staff met with several National Correspondents and had useful discussions with them regarding more effective methods of co-operation. IRPTC is very grateful to all National Correspondents for the contribution and continued assistance in the development of IRPTC.

The number of National Correspondents stands at 119 from 111 countries.

The Query-Response Service

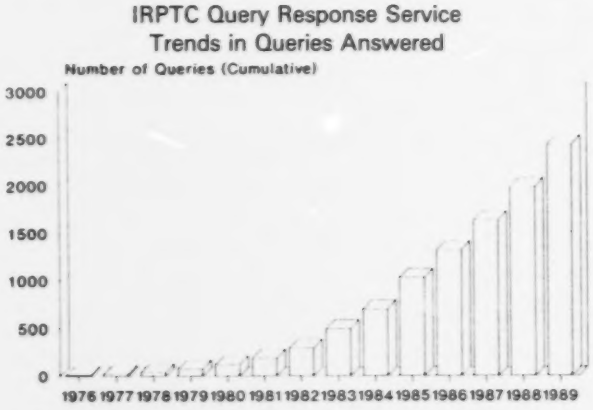
IRPTC has operated a Query-Response Service since the receipt of its first request for information in March 1976. Many changes to streamline and speed up the process of answering questions have been implemented since its formal inception later in that same year.

The latter half of 1989 has seen the entry into service of a personal computer database to register and keep record of the incoming requests for assistance received on a daily basis at IRPTC. It is hoped that this will make the running of the Query-Response Service more simple and efficient.

Although the service began at a moderate rate of 11 queries per year, it has now reached a level where an average of 1 query is received per day at the Programme Activity Centre in Geneva. The growth figures are given in the table below and are depicted in the accompanying graphical representation.

Queries received by IRPTC (1976-1989)

Year	Yearly total	Cumulative total	Mid-Year
1976	11	11	7
1977	11	22	28
1978	19	41	23
1979	34	75	50
1980	46	121	97
1981	69	190	148
1982	105	295	234
1983	197	492	384
1984	201	693	596
1985	335	1028	866
1986	292	1320	1170
1987	312	1632	1488
1988	350	1982	1810
1989	450	2432	2203



The number of queries does not necessarily indicate the number of chemicals to which IRPTC responds since a single query may request information for as many as 30 chemicals. A further characterization of the queries is provided in the following table (expressed as percentages of the total number of queries received up to 30 November 1989):

developing/developed countries	50%/50%
environmental/non-environmental	31%/69%
agrochemical/non-agrochemical	30%/70%
legal matters	23%
waste matters	13%

Since the beginning of 1989, a new field has been added to the subject breakdown of queries, namely hazardous waste matters. Most people are aware of the controversy

that has been recently stirred on this topic and the Query-Response Service is already beginning to reflect this awakening of public interest.

The Query-Response Service handles such varied requests for information as the waste problem related to disposable nappies, the environmental toxicity problem of chemical spills occurring at sea and the food contamination hazards of caviar! This is to mention a small selection of the variety of questions received at IRPTC.

The Query-Response Service uses primarily its own computerized database on chemicals to answer questions but often must go beyond this source. Insufficient data or lack of a profile leads IRPTC to outside collaborators to obtain complementary material. These may be specific to the request i.e., WHO for public health related questions, IARC for carcinogenicity, UNEP's Industry and Environment Office for questions related to industrial technology and so on. Other sources include the IRPTC network of National Correspondents, intergovernmental organizations, non-governmental organizations and cooperating partners including industry. Computerized bibliographical databases with which IRPTC is linked may also be consulted.

Although IRPTC is designed primarily to aid national authorities responsible for the protection of human health and the environment, its services are available to everyone.

At present the Query-Response Service is still free of charge. Although it has been suggested that a fee be charged for the provision of data profiles there is concern that this would deter queries, particularly those from the developing countries. These are the users IRPTC is most anxious in establishing and retaining as they generally have the least access to other services of information.

The same collaborators that IRPTC may contact for information are included in the list of those that use the Query-Response Service, in addition to research centres, academia, governmental departments and agencies, and private individuals.

The IRPTC National Correspondents also play an essential role in the operation of the Query-Response Service. Sometimes they are able to handle a query themselves or through information sources in their country; otherwise they refer the query to the IRPTC central unit.

The Query-Response Service benefits more that just its users; it is also of value to the IRPTC staff as it identifies gaps in the information available and is often an incentive to complement and/or update the information existing in a data profile and hence provide the best possible information to its users.

London Guidelines 'Prior Informed Consent'

The Governing Council of UNEP by its decision 14/27 of 17 June 1987 adopted the London Guidelines for the Exchange of Information on Chemicals in International Trade. Furthermore, by the same decision, the Governing Council requested the Executive Director of UNEP to convene an *Ad hoc* Working Group of Experts to develop modalities of Prior Informed Consent (PIC), and other approaches which could usefully supplement the London Guidelines and to recommend ways of incorporating the principle of Prior Informed Consent into the Guidelines (Bulletin Vol. 9 No. 1).

The first session of the *Ad hoc* Working Group on Prior Informed Consent and Other Modalities to Supplement the London Guidelines for the Exchange of Information on Chemicals in International Trade was held in Dakar (Senegal) from 19 to 23 September 1988. The second session was held at the United Nations Headquarters in New York from 13 to 17 February 1989 and was attended by experts nominated by 27 developed and developing countries, and observers from the United Nations bodies, intergovernmental organizations, non-governmental organizations and chemical industry associations of Europe, Japan and the United States.

The second session was opened by Dr Mostafa K. Tolba, the Executive Director of UNEP. In his opening address, Dr Tolba made a number of important comments and recommendations to the Working Group for consideration.

The Working Group considered and discussed the proposal for incorporating PIC into the London Guidelines which had been worked out on the basis of the deliberations of the Working Group at its first session. It noted that UNEP and FAO are both developing PIC procedures which should be developed in a complementary fashion and should not duplicate each other.

The Working Group recommended that the Executive Director of UNEP should propose to the Governing Council of UNEP at its fifteenth session in May 1989 that it:

(a) Adopt the revised London Guidelines as amended by the Working Group;

(b) Recommend that UNEP and FAO develop an information exchange system for obtaining information and communicating decisions on chemicals subject to PIC procedures and jointly manage and implement common elements, including the selection of chemicals to be included in the PIC procedure and preparation of PIC decision guidance documents.

In considering the incorporation of the concept of the PIC into the London Guidelines, the Working Group agreed that this concept refers to the principle that international shipment of a chemical that is banned or severely restricted in order to protect human health or the environment should not proceed without the agreement, where such agreement exists, or contrary to the decision, of the Designated National Authority in the importing country. The Working Group further agreed that the term 'Prior informed consent procedure' (PIC procedure) should be defined as the procedure for formally obtaining and disseminating the decisions of importing countries as to whether they wish to receive future shipments of a specific chemical which has been banned or severely restricted. PIC decision guidance documents were requested for each chemical. A specific procedure was established for selecting chemicals for initial implementation of the PIC procedures. These include chemicals which have been previously banned or severely restricted as well as certain pesticide formulations which are acutely toxic. This is explained in an annex to the Guidelines and is summarized below.

(1) All Designated National Authorities in all States should submit inventories of control actions, in accordance with the Guidelines, to IRPTC if they have not already done so. Submissions should be made as soon as possible to be available in IRPTC prior to the date of implementation of the PIC procedure.

(2) On the basis of these submissions, IRPTC will identify all chemicals banned or severely restricted by five or more countries. These will be introduced into the PIC process according to the following criteria:

(a) All chemicals banned or severely restricted as defined in these Guidelines, by ten or more countries should be immediately placed on a list and circulated, with PIC decision guidance documents, to countries participating in these Guidelines for determination regarding future use and importation;

(b) Chemicals banned or severely restricted by five or more countries, but by less than ten, should be submitted to an informal consultation to determine whether they meet the definitions of banned and severely restricted for human health or environmental reasons. This determination should be made as expeditiously as possible. Those chemicals that meet the definitions will be circulated as an addition to the list referred to in subparagraph (a) above, with PIC decision guidance documents, for a determination by participating importing countries regarding their future use and importation.

(3) Should additional inventories of past control actions be received by IRPTC subsequent to the implementation date of the PIC procedures, they will be added to the original inventory. This updated inventory should be assessed annually in the same manner as the original inventory as above and incorporated into the PIC procedure as appropriate. These additional chemicals should be circulated to participating importing countries for their consideration and determination regarding future use and importation under the PIC procedure.

As regards acutely toxic pesticide formulations, the Working Group recommended that an Expert Group composed of representatives from WHO, FAO and UNEP as well as pesticide registrars will review pesticide formulations based on the WHO Class 1A compounds to determine if there is a need for a list of such products to supplement the chemicals already subject to the PIC procedure. This new Expert Group may call upon the expertise of industry and non-governmental organizations and other experts as they deem necessary. The group may conclude that there are actually hazardous pesticide formulations of concern to developing countries which are not already included in the PIC procedure. A supplementary list of such formulations will then be recommended for inclusion.

On the recommendation of the *Ad hoc* Working Group and on the proposal of the Executive Director, the Governing Council of UNEP in its decision 15/30 of 25 May 1989 adopted the amended London Guidelines for the Exchange of Information on Chemicals in International Trade. The following is the text of this decision:

15/30. Environmentally safe management of chemicals, in particular those that are banned and severely restricted, in international trade

The Governing Council,

Recalling its decision 85 (V) of 25 May 1977, in which it urged Governments to take steps to ensure that potentially harmful chemicals, in whatever form or commodity, which are unacceptable for domestic purposes in the exporting country, are not permitted to be exported without the knowledge and consent of appropriate authorities in the importing country,

Further recalling its decision 14/27 of 17 June 1987, by which the Council adopted the London Guidelines for the Exchange of Information on Chemicals in International Trade, which constitute an important step towards the full implementation of decision 85 (V), and requested the Executive Director to convene an *Ad hoc* Working Group of Experts with a view to:

(a) Developing modalities of prior informed consent and other approaches which could usefully supplement the modalities of the London Guidelines;

(b) Recommending measures for incorporating the principle of prior informed consent into the Guidelines;

(c) Reporting on its findings to the fifteenth session of the Council.

1. *Takes note with appreciation* that, in accordance with decision 14/27, the *Ad hoc* Working Group of Experts on Prior Informed Consent and Other Modalities to Supplement the London Guidelines for the Exchange of Information on Chemicals in International Trade has completed its work as requested;

2. *Notes* that the United Nations Environment Programme and the Food and Agriculture Organization of the United Nations are both developing prior informed consent procedures, which should be developed in a complementary fashion and should not duplicate each other;

3. *Notes also* that the prior informed consent procedure being developed by the Food and Agriculture Organization of the United Nations in the context of the International Code of Conduct on the Distribution and Use of Pesticides is expected to be fully compatible with that in the amended London Guidelines both procedurally and with respect to health and environmental protection, and is expected to be approved prior to full implementation of the prior informed consent procedure as contained in the amended London Guidelines;

4. *Further notes* that the increased workload for the United Nations Environment Programme as the amended London Guidelines are implemented would imply the need for additional resources;

5. *Adopts* the amended London Guidelines for the Exchange of Information on Chemicals in International Trade;

6. *Recommends* that the Expert Group to be established pursuant to annex II, paragraph 2 of the amended London Guidelines, keep the issue of acutely hazardous pesticide formulations under continuing review after completion of its initial task as outlined in annex II with a view to formulating any recommendations for additional action in this regard as may be appropriate to the *Ad hoc* Working Group of Experts when it is re-convened by the Executive Director to monitor the implementation of the London Guidelines;

7. *Recommends* that the United Nations Environment Programme and the Food and Agriculture Organization of the United Nations develop an information exchange systeme to ensure that Designated National Authorities of importing and exporting countries have a single contact point for obtaining information and communicating decisions on chemicals subject to the prior informed consent procedure;

8. *Recommends* that the United Nations Environment Programme and the Food and Agriculture Organization of the United Nations share the operational responsibility

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for the implementation of the prior informed consent procedure and jointly manage and implement common elements, including the selection of chemicals to be included in the prior informed consent procedures, preparation of prior informed consent decision guidance documents, mechanisms for information-sharing, and creation of data bases;

9. *Expresses its understanding* that the sharing of operational responsibilities referred to above is without prejudice to the scope of the Guidelines as defined in paragraph 1 (a) of the Guidelines;

10. *Calls upon* the Conference of the Food and Agriculture Organization of the United Nations to adopt procedures equally protective for man and the environment for pesticides subject to the prior informed consent procedure;

11. *Requests* the Executive Director to re-convene the *Ad hoc* Working Group with a view to:

(a) Monitoring, as appropriate and within available resources, the implementation of the amended London Guidelines, with particular attention to the prior informed consent procedure and the technical assistance provisions of Part III of the Guidelines;

(b) reviewing other activities related to the production and use of chemicals in States specifically including the work of the Food and Agriculture Organization of the United Nations on integrated pest management and in implementing the International Code of Conduct on the Distribution and Use of Pesticides, the work of the United Nations Environment Programme in conjuction with industry on chemical management and safety issues, and the experience of the United Nations Environment Programme and the Organisation for Economic Co-operation and Development on information exchange, chemicals control and developing and implementing conventions or agreements on transboundary movement of hazardous waste;

(c) On the basis of such monitoring and review, preparing a report on any further steps which should be taken to supplement the amended London Guidelines, including the possible further need for a convention, for submission to the Governing Council at its sixteenth regular session;

12. *Urges* Governments to take the necessary steps for the early implementation of the London Guidelines.

As chemicals defined in the London Guidelines include both industrial chemicals and pesticides, the joint responsibility of UNEP and FAO in operating the PIC procedure has been identified in the amended London Guidelines and the Governing Council decision 15/30. Since the adoption of decision 15/30, UNEP and FAO have exchanged letters and confirmed mutual co-operation on the implementation of the PIC procedure. The principle of PIC has also been incorporated in the International Code of Conduct on the Distribution and Use of Pesticides of the FAO by the 25th session of the FAO Conference in November 1989. A FAO/UNEP joint programme for the operation of the PIC procedure is in the final stages of preparation by IRPTC and FAO. A Memorandum of Understanding between UNEP and FAO has been drafted and is being discussed with FAO.

Plans to hold technical workshops and awareness campaigns on this subject are being discussed between IRPTC and FAO. UNEP and FAO have written identical parallel letters to all Governments to designate national authorities for the implementation of the PIC procedure.

Copies of the amended London Guidelines as adopted by the Governing Council are available upon request from: The Director, IRPTC/UNEP, Palais des Nations, CH-1211 Geneva 10, Switzerland.

UNEP Governing Council: 15th Session

The fifteenth session of UNEP Governing Council was held at UNEP Headquarters in Nairobi, Kenya, from 15 to 26 May 1989. One hundred and three countries attended this session. This was a record number as was the number of Ministers, forty-four in all, who actively participated.

The Council approved a target of US$100 million for UNEP 1992. 'This is a 250% increase in UNEP funding', Dr. Mostafa K. Tolba, Executive Director of UNEP, declared with satisfaction.

The decisions taken by the Council included:

—A global climate treaty should be a top UNEP priority.
—Work will begin without delay on a treaty to conserve biological diversity.
—The focus of UNEP's activities was narrowed so that they would be much more effective.

Eight proposed 'Areas of Concentration' were agreed upon. These were:

—protection of the atmosphere by combating climate change and global warming, depletion of the ozone layer, and transboundary air pollution,
—protection of the quality of fresh-water resources,
—protection of ocean and coastal areas and resources,
—protection of land resources by combating deforestation and desertification,
—conservation of biological diversity,
—environmentally sound management of biotechnology,
—environmentally sound management of hazardous wastes and toxic chemicals and protection of human health conditions,
—emphasis on the quality of life, especially the living and working environment of poor people.

In addition the importance of aid to developing countries won approval of the Council. It was also emphasized that 'sustainable' development in developing countries cannot be used by industrialized societies to impede development or to dictate it. It was also agreed that UNEP's role inside the UN system and outside in the world must be strengthened.

IRPTC

The work of IRPTC and its related activities were discussed in the context of UNEP's programme on environmental assessment.

In his introductory statement, the Assistant Executive Director of UNEP noted that the responsibilities of the International Register of Potentially Toxic Chemicals (IRPTC) has increased with the growth in international trade in chemicals; its network of National Correspondents now covered 111 countries. He noted further that IRPTC operated a databank and a global network for the exchange of information on potentially toxic chemicals and was co-

operating closely with other international organizations, in particular with the International Programme on Chemical Safety (IPCS). IRPTC participated in IPCS Task Group meetings and provided data to them. The Register also operated a query-response service and was an INFOTERRA special sectoral source for scientific and regulatory information on chemicals. The Assistant Executive Director also mentioned the important role IRPTC had played in the preparation of the Basel Convention, the further development of the London Guidelines and the incorporation of the principle of Prior Informed Consent (PIC). IRPTC was assisting developing countries in establishing National Registers of Potentially Toxic Chemicals and provided training to them.

All representatives who spoke on IRPTC expressed great appreciation of the subprogramme's efforts to provide valid data on chemicals. Several representatives commended IRPTC as a valuable resource; one said that IRPTC had greatly assisted in the implementation of the London Guidelines, in developing a national register and in providing training within his country.

One representative stated that co-operation between IRPTC and IPCS should continue and indicated his country's willingness to continue to provide data to these programmes. Another representative also supported continued co-operation between these programmes particularly in the area of training.

In expressing their support for IRPTC, all representatives said that is should remain a high priority. Several noted that additional resources would be needed to meet the increased responsibilities of IRPTC, in particular those related to implementing the London Guidelines in their amended form, as well as training.

Several representatives endorsed the recommendation of the expert consultation on IRPTC for soliciting extrabudgetary resources. They also supported IRPTC's amended objectives and strategies.

Given the new responsibilities to which these gave rise, some representatives indicated that they might provide additional support to IRPTC. Suggesting areas for possible improvements, one representative noted the need to strengthen the databank on chemicals and to consider providing assistance to developing countries in computer science and technology. Several requested a stronger training programme that would increase the participation of officials from developing countries. One expressed his satisfaction with the co-operation between IRPTC and the Centre for International Projects of UNEPCOM in this area, and urged industrialized countries to develop similar co-operative arrangements for training.

Several representatives expressed support for the initiative to establish national registers of potentially toxic chemicals, others noted the need to strengthen the IRPTC network of National Correspondents, and yet another encouraged Governments and industry to contribute information to IRPTC in a usable form.

One representative noted the report on the list of environmentally harmful chemicals but expressed concern at the increased demands on the UNEP budget and on Governments that might result.

All representatives who spoke on the proposed amendment to the London Guidelines concerning PIC expressed support for its adoption, but most noted the need to ensure full co-operation with FAO. All but one however considered the development of a convention on trade in potentially toxic chemicals premature.

Furthermore, it was noted that IRPTC must be able to assist developing countries in implementing PIC procedures. In this respect the observer for FAO mentioned his organization's continuing close co-operation with UNEP.

Commenting on the successful completion of the Basel Convention, several representatives referred to IRPTC's role in its implementation. One stressed the need for close co-operation between the Register and the interim secretariat of the Convention.

At the conclusion of the debate the Governing Council adopted the following decisions on IRPTC:

15/28. International Register of Potentially Toxic Chemicals

The Governing Council,

Recalling its decision 14/19 of 17 June 1987, on the International Register of Potentially Toxic Chemicals,

Having considered the report of the Executive Director on the International Register of Potentially Toxic Chemicals,[65]

Noting the recommendation in the recent report that the International Register of Potentially Toxic Chemicals, should support developing countries in establishing national registers of potentially toxic chemicals,[66]

Noting the need to ensure close co-operation among the International Register of Potentially Toxic Chemicals, the Industry and Environment Office, and the interim Secretariat of the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal, in particular to make the best use of available resources,

1. *Takes note* of the information on the short-term and long-term financial position of the Register provided by the Executive Director in his report;
2. *Requests* the Executive Director to continue to give high priority to the work of the Register through full and flexible utilization of:

(a) The resources of the Fund;
(b) Additional sources of income, and also through coordination with other related budget subprogrammes;

3. *Also requests* the Executive Director to solicit extrabudgetary resources from Governments in the form of counterpart contributions to cover the resource needs of the Register and prepare package programmes for the different activities;
4. *Invites* the Executive Director to submit such programmes to potential donors for financing;
5. *Approves* the revised objectives and strategies of the Register, to reflect accurately its expanded responsibilities, as contained in the annex to the present decision;
6. *Invites* the Executive Director to strengthen the International Register of Potentially Toxic Chemicals, within available resources and extrabudgetary resources, in accordance with its new mandate to assist developing countries at their request in the field of legal and institutional arrangements for the management of chemicals at the national level and to organize training activities.

[65] UNEP/GC.15/9/Add.2/Supplement 1, paras. 1-10.

[66] *Ibid.*, para. 9.

ANNEX

Revised Objectives and Strategies of the International Register of Potentially Toxic Chemicals (IRPTC)

A. Objectives

1. To facilitate access to existing data on the production, distribution, release and disposal of chemicals, and their effects on man and his environment, and thereby contribute to a more efficient use of national and international resources available for the evaluation of the effects of the chemicals and their control.

2. On the basis of information in the Register, to identify the important gaps in existing knowledge on the effects of chemicals, and call attention to the need for research to fill those gaps.

3. To identify, or help identify, potential hazards from chemicals and wastes, and to improve the awareness of such hazards.

4. To provide information about national, regional and global policies, regulatory measures and standards and recommendations for the control of potentially toxic chemicals.

5. To facilitate the implementation of policies necessary for the exchange of information on chemicals in international trade.

B. Strategies

1. Rendering the IRPTC Programme Activity Centre capable of handling data and answering questions.

2. Involving correspondents designated at the national, regional and sectoral levels in the operations of IRPTC.

3. Building a network of participating data systems, which may make their files available to the IRPTC Programme Activity Centre for incorporation in its central data files, or may respond directly to user's queries.

4. Developing and continuously updating computerized central data files.

5. Publishing selected information on chemicals.

6. Assisting with the strengthening of legal and institutional arrangements for the management of chemicals at the national level.

7. Developing for use within IRPTC and at the national level and amending when necessary, procedures and programmes needed to make the London Guidelines effective.

8. Co-ordinating the reporting and information exchange under the London Guidelines among participating Governments and relevant intergovernmental and non-governmental organizations.

9. Reviewing and periodically reporting progress and problems related to the implementation of the London Guidelines.

10. Promoting the use of outputs from IRPTC activities.

11. Organizing training activities.

12th Meeting
25 May 1989

Source: United Nations Environment Programme. 'Proceedings of the Governing Council at its Fifteenth Session, Nairobi, 15-26 May 1989.' (UNEP/GC.15/12. July 1989.)

Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal

The Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal was adopted unanimously on 22 March 1989 by the 116 States participating in the Conference of Plenipotentiaries on the Global Convention on the Control of Transboundary Movements of Hazardous Wastes, which was convened by the Executive Director of the United Nations Environment Programme (UNEP) and held in Basel at the invitation of the Government of Switzerland. The Final Act of the Basel Conference was signed by 105 States and the European Economic Community (EEC).

The Conference was convened pursuant to Governing Council decision 14/30 of 17 June 1987, by which the Council approved the Cairo Guidelines and Principles for the Environmentally Sound Management of Hazardous Wastes (UNEP/GC.14/17, annex II) and authorized the Executive Director to convene a working group of legal and technical experts to develop a global convention on the control of transboundary movements of hazardous wastes.

The Basel Convention is the result of six sessions of the *Ad hoc* Working Group (Budapest, 27-29 October 1987, (organizational meeting); Geneva, 1-5 February 1988 ; Caracas, 6-10 June 1988; Geneva, 7-16 November 1988; Luxembourg, 30 January-3 February 1989; and Basel, 13-17 March 1989), in which experts from 96 States and representatives of over 50 organizations participated. Informal negotiations conducted by the Executive Director with governments, organizations and industry also played an important part in the success of the preparatory process.

Forty-one States and the EEC have signed the Basel Convention. Two countries have ratified (by 31.12.89). It will enter into force upon ratification by twenty States.

The provisions of the Convention include the following:

(a) The generation of hazardous wastes as well as their transboundary movements shall be reduced to a minimum. The wastes should be disposed of as close as possible to their source of generation.

(b) Every State has the sovereign right to ban the import of hazardous wastes. The Parties to the Convention shall not allow any transboundary movement of hazardous wastes to a State that has prohibited their import. Transboundary movements shall also be prohibited if the exporting State has reason to believe that the wastes in question shall not be managed in an environmentally sound manner.

(c) A party shall not permit hazardous wastes to be exported to a non-Party or to be imported from a non-Party, unless it is in accordance with a bilateral, multilateral or regional agreement, the provisions of which are no less environmentally sound than those of the Basel Convention.

(d) The State of export shall not allow a transboundary movement of hazardous wastes to commence until it has received the written consent, based on prior detailed information of the State of import, as well as of any State of transit that has not informed the Convention Secretariat of its decision to require no prior written consent for transboundary movements of hazardous wastes.

(e) When a transboundary movement of hazardous wastes which is carried out in accordance with the Convention cannot be completed in an environmentally sound manner, the State of export has the duty to ensure the re-importation of the wastes.

(f) Transboundary movements of hazardous wastes which do not conform to the provisions of the Convention are deemed to be illegal traffic. The Convention states that 'illegal traffic in hazardous wastes is criminal'. The State responsible for an illegal movement of hazardous wastes has the obligation to ensure their environmentally sound disposal, by re-importing the wastes or otherwise. Every Party shall introduce national legislation to prevent and punish illegal traffic in hazardous wastes.

The wastes covered by the Convention are defined in its annexes. Hazardous wastes subject to transboundary movement must be packaged, labelled and transported in conformity with generally recognized international rules and standards. Since the authorities of many countries, especially developing ones, frequently do not have the trained specialists and technical know-how to assess information concerning hazardous wastes and handle it efficiently, the Convention calls for international co-operation involving, among other things, the training of technicians, the exchange of information, and the transfer of technology. Guidance materials to assist countries in using the technical annexes are to be prepared.

The Convention provides for the establishment of a Secretariat, the main functions of which shall be to process and disseminate information provided to it by the Parties, to ensure co-operation between Parties, and to provide assistance to them in implementing the Convention.

The Convention provides that UNEP will carry out the Secretariat functions on an interim basis, pending the first meeting of the Parties to the Convention after its entry into force. These functions will include undertaking activities in accordance with the resolutions adopted by the Basel Conference. One of these resolutions called upon all States to become Parties to the Convention and to take actions in accordance with its provisions even before its entry into force. In another, the Conference requested the Executive Director of UNEP to take the necessary steps for the Interim Secretariat to commence its activities as soon as possible, and called upon Governments to contribute financially towards its costs. In this connection, the Executive Director of UNEP has presented preliminary budget estimates and stated UNEP's willingness to contribute towards the costs of the Interim Secretariat during its initial two years of the operation. The Interim Secretariat for the Basel Convention (ISBC) has been established and commenced its activities in November 1989.

The Final Act of the Conference and the Basel Convention are available upon request from the: United Nations Environment Programme (UNEP), P.O. Box 30552, Nairobi, Kenya; and the Interim Secretariat of the Basel Convention (ISBC), c/o UNEP, Palais des Nations, 1211 Geneva 10, Switzerland.

Industry and Environment Office

Awareness and preparedness for emergencies at local level

In late 1986, following various industrial accidents that occurred in both highly industrialized and industrializing countries, resulting in adverse impacts on the environment, the United Nations Environment Programme (UNEP) suggested a series of measures to help governments, particularly in developing countries, minimize the occurrence and harmful effects of chemical accidents and emergencies. In particular, even if it is believed that all industrial accidents are preventable, one must be realistic enough to prepare response plans in the event that such accidents occur. Such preparation should lead to a better understanding of local hazards, and thus to preventive actions.

In this context, the UNEP Industry and Environment Office has developed, in co-operation with industry, a 'Handbook on Awareness and Preparedness for Emergencies at Local Level (APELL)', designed to assist decision-makers and technical personnel in improving community awareness of hazardous installations, and in preparing response plans should unexpected events at these installations endanger life, property or the environment. UNEP is aware that in all countries as well as internationally, provisions are made for emergency planning for natural as well as for technological disasters and accidents. This handbook is not intended to replace or interfere with such provisions of national law or of national and international activity, but rather to increase generally the knowledge of such provisions, responsibilities and activities.

In an introductory chapter, the background, approach and the scope of the APELL Process are presented. The thrust in this handbook is directed at the local level, since recent evidence shows that the extent of an accident's impact depends heavily on the immediate response to an emergency at the plant site and at the local level. APELL also recognizes the role of State or Federal levels of governments in setting national goals, priorities or regulations and in providing the support and resources that local communities need.

This Handbook is designed to address and respond to the emergency events associated with any industrial or commercial operation as the results of fire, explosion, spills or release of hazardous materials. However, it has not been the intention to address emergencies related to nuclear energy or military activities. It provides the basic concepts for the development of action plans based on local community awareness of potential dangers, and the preparation of emergency response plans at the local level, as well as an overall framework of the organizational structure. Although the objectives remain unchanged, the tools suggested are flexible, and the mechanics of the operation can be adapted to specific local conditions and requirements.

In the second chapter, the main objectives and the basic concepts of the APELL Process are described: the overall goal is to prevent loss of life and property, and to ensure environmental safety in the community. Two basic approaches are used: (i) to increase knowledge in the community about the possible risks and hazards in the area, and (2) to develop, on the basis of this information, coordinated emergency response plans.

At the local level there are three very important partners who must be involved if APELL is to succeed: (i) *Local authorities:* these may include province, district, city or town officials, either elected or appointed, who are responsible for safety, public health and environmental protection in their area. (ii) *Industry:* industrial plant managers from either State-owned or private companies are responsible for safety and accident prevention in their operations. They prepare specific emergency preparedness

measures within the plant and establish review of the industrial plant's operation. But their responsibilities do not stop at the fence. As leaders of industrial growth and development, they are in the best position to interact with local authorities and leaders, to provide awareness on how the industrial facility operates, and on how it could affect its environment and to help prepare appropriate community response plans in the event of an emergency. The involvement and active participation of the work force is also important. (iii) *Local community and interest groups:* for example environmental, health, lay care, media, and religious organizations, and leaders in the educational and business sectors that represent the concerns and views of their constituents in the community.

At the national level, governments have an important role to provide the co-operative climate and support under which local participants can achieve better preparedness. Through leadership and endorsement, national authorities should foster participation of everyone at the local level. Industry associations should also get involved. There are other partners and the APELL Process is designed so as to harmonize with other initiatives and efforts in reducing risk and hazards as well as their consequences.

The third chapter explains how to start the APELL Process. Local authorities, community leaders and industrial representatives need to build a bridge for co-operation among all partners at the local level. This can be done by the formation of a Co-ordinating Group to provide close and direct interaction between industry, the local community and the community leaders. All groups with an interest in the planning process should be included. The Co-ordinating Group will be the focus for a unified and co-ordinated approach to emergency response planning and communication with the community. This group has the responsibility to gather facts and opinions, assess risks, establish priorities, evaluate approaches and generally organize the personnel in the community and the resources available to produce emergency response as part of overall emergency preparedness. Any group can be the catalyst to initiate the APELL Process and to establish the Co-ordinating Group. Once this has been done a 'leader' should be selected whose primary responsibility will be to conduct the group's efforts through the various phases of its work.

The fourth chapter deals specifically with community awareness. It refers first to the need for and the right of the local community to be informed about and to participate at all times in response planning for hazardous installations. There is really nothing mysterious about a community awareness programme. A fenced-in industrial plant can look threatening to the public; but much of the mystery disappears when people know what the plant uses and manufactures, that it has a good safety plan and safety record, and that an effective emergency plan exists.

No one can prescribe the activities necessary for a local awareness programme that will fit every industrial facility or complex at every location. However, the handbook describes actions that plant managers, local authorities and community leaders might take, individually or within the Co-ordinating Group, to improve local awareness. The fourth chapter also provides some basic techniques for information exchange and communication.

The last chapter outlines the APELL planning process that can be used to achieve a high level of preparedness for emergencies at the local community level. It describes key issues to be addressed in the process and suggests a 10-step approach to plan for emergencies. A checklist useful for completing each step is given as well as some industry experience.

The handbook is designed to provide national governments, local authorities and plant managers guidance on building greater awareness of hazardous installations in a local community, and on preparing co-ordinated emergency plans. Since the containment of health and environmental impacts depends upon the speed and scope of the initial local response, the emphasis in this document is directed to local level participation. The document recognizes however the fundamental roles of national governments, ministries, and chief executive officers of industries to support and assist these efforts at the local level.

Source: 'Awareness and Preparedness for Emergencies at Local Level (APELL)'. Industry and Environment Office, United Nations Environment Programme, 39-43 Quai André Citroën, 75739 Paris Cedex 15, France (1988).

Chemicals in the Environment

Environmental Objectives: Reduce to an acceptable or, if possible, to a negligible level the risks posed to humans and the environment by individual or groups of substances. This means that for certain substances emissions must be reduced by 50 to 70%.

Source: National Environmental Policy Plan for The Netherlands. (1989).

II. International and National Activities

International Agency for Research on Cancer

I. Man-made mineral fibres

The forty-third volume of IARC Monographs comprises four monographs: three on man-made mineral fibres (glass fibre, rockwool and slagwool and ceramic fibres) and one on gas (radon). Previous monographs have evaluated the carcinogenicity of other man-made fibres: asbestos, silica, woolastonite, attapugite, talc, erionite and sepiolite.

'Man-made mineral fibres' is a generic term denoting fibrous inorganic substances made primarily from rock, clay, slag or glass. These fibres can be classified into three general groups: glass fibres (comprising glasswool and glass filament), rockwool and slagwool, and ceramic fibres.

Synonyms and trade names

Glasswool: JM (Johns Manville) 100; JM 102; JM 104; JM 110
Glass filament: ES 3; ES 5; ES 7.
Rockwool: G + H
Slagwool: RH; ZI
Ceramic fibre: Fiberfrax; Fibermax; Fireline Ceramic; Fybex; MAN; Nextel; PKT; Saffil.

Glass fibres (glasswool and glass filament)

Glass fibre is produced either as glasswool or glass filament. Glasswool is produced by drawing, centrifuging or blowing molten glass and comprises cylindrical fibres of relatively short length (compared to filaments). Glass filaments are continuously drawn or extruded from molten glass. This class of materials includes longer, large-diameter filaments for textile and reinforcing applications as well as fine-diameter filaments.

Rockwool and slagwool

Rockwool and slagwool are produced by blowing, centrifuging or drawing molten rock or slag. Rockwool is typically made from igneous rocks such as diabase, basalt and olivine, and carbonate rocks containing 40-60% calcium and magnesium carbonates. Rockwool remains in the glassy state because it is cooled so rapidly that it does not recrystallize. It dissolves in dilute hydrochloric acid. Slagwool is made from the fused agglomerate by-products of certain metal smelting processes; its composition is thus a reflection of the range of components in the different slags used in the melt. The properties of the fibre vary not only according to the sources of raw material but also from batch to batch.

The overwhelming majority of glasswool, rockwool and slagwool produced is used for thermal and acoustical insulation applications in construction and shipbuilding. Approximately 80% of the glasswool produced for structural insulation is used in houses. Rockwool and glasswool in the form of loose-bagged wool, is pneumatically blown or hand-poured into structural spaces. Bulk rockwool and glass-fibre rovings are incorporated into ceiling tiles for fire resistance and thermal and sound insulation. Batts, blankets and semi-rigid boards made of glass or rockwool and slagwool fibres are commonly used between structural members of residential and commercial buildings. In addition, glass fibres have a number of other uses such as aerospace engineering, roofing or surfacing tissue, vehicle bodies, and tyre reinforcement. Continuous filament fibre glass is used as a conductor of light (fibre optics), for communications, light and image transmission and decoration.

Ceramic fibres

Ceramic fibres comprise a wide range of amorphous or crystalline, synthetic mineral fibres characterized by their refractory properties (i.e. stability at high temperatures). Ceramic fibres are typically made of alumina, silica and other metal oxides or, less commonly, of nonoxide materials, such as silicon carbide. Most ceramic fibres are composed of alumina and silica in an approximate 50/50 mixture.

Ceramic refractory fibres are also used as insulation materials. Due to their ability to withstand high temperatures, they are used primarily for lining furnaces and kilns. End-products may be in the form of blankets, boards, felts, bulk fibres, vacuum-formed or cast shapes, paper and textile products. Their light weight, thermal shock resistance and strength make them useful in a number of industries.

Characterization of man-made mineral fibres

Physicochemical characterization of a sample is essential when testing fibrous particulates for biological activity, for two reasons: (i) to ensure that the sample to be tested is representative of the materials to which humans are exposed; and (ii) to permit evaluation of specific physical and chemical characteristics of the fibres which may be important in the induction of cancer. It is important that sufficient numbers of fibres from each sample to be tested for carcinogenicity be measured using methods that allow detection of both submicroscopic and microscopic fibres, so that the number of fibres of specific dimensional categories per unit mass can be calculated.

When characterizing exposures to man-made mineral fibres, it is necessary to specify the distributions of fibre diameters and lengths, as well as the total number of fibres per unit volume of air in order to lay a foundation for dose-response relationships. The most desirable reporting mode for research purposes is in numbers of fibres per unit volume in size classes of diameter and length. In the studies reported in this monograph, such information was not always available. For the purposes of occupational safety, the number of fibres per unit volume in a given size and length class is usually specified.

The composition of bulk material and the fibre sizes vary widely among and within each fibre category, i.e., glass, rock, slag and ceramic. Therefore, specifications of bulk material should accompany data on exposure whenever possible. Trade names broadly classify bulk material with regard to composition and to distribution of fibre diameter

and length; but airborne fibres released by bulk materials vary greatly in diameter and length, even within a single trade designation.

Man-made mineral fibres break predominantly across the fibre axis. They do not form fibrils, as does chrysotile. These differences in breakage characteristics explain why chrysotile in air is associated with a large number of submicro-size fibres, while airborne man-made mineral fibres are not. Optical microscopy can be used for routine assessment of man-made mineral fibres (length, >5 μm) in work places. Detailed analysis of size and determination of the elemental composition of all man-made mineral fibres except very fine fibres can be performed with a scanning electron microscope. Analysis of very fine fibres requires transmission electron microscopy.

Routes of exposure to mineral fibres

Inhalation is the major route of exposure to mineral fibres that have been shown to cause cancer in humans (e.g., asbestos). Therefore, it is desirable to use the inhalation route, if possible, when testing such fibres for their carcinogenicity in animals; however, the qualitative and quantitative aspects of particle deposition and retention in rodents are considerably different from those in humans. As a result, particles that may be important in the induction of disease in humans may never reach the target tissues in sufficient quantities in rodents. This problem cannot be overcome by generating higher concentrations of particulate aerosols because of technical complications, e.g., particle aggregation. The consequence is that inhalation tests may be less sensitive than tests by other routes for evaluating the carcinogenicity of particulate and fibrous materials. In addition, the high cost and the shortage of adequate facilities for such studies severely limit the number that can be performed.

It is thus often necessary that other routes of administration be used for testing the carcinogenic potential of mineral fibres. The methods that have been most frequently employed are intratracheal instillation and intrapleural and intraperitoneal administration. With the first, various lung tissues as well as the pleural mesothelium are the major targets for the administered test fibres; in the latter two, the pleural and the peritoneal mesothelium, respectively, are the target tissues. These routes of administration can be used to test the carcinogenicity of mineral fibres to laboratory animals because they bring the test fibres into intimate contact with the same target tissues as in humans.

Mechanisms of fibre carcinogenicity

In this monograph, man-made mineral fibres are divided into five groups, according to the materials from which they are produced or to the manufacturing process. The groups are: glasswool, glass filament, rockwool, slagwool and ceramic fibres. The major fibre characteristics, based on current knowledge, that are likely to be determinants of the adverse biological effects of fibres are: (i) fibre length, (ii) fibre diameter, and (iii) *in vivo* durability and persistence, i.e., the ability of a fibre to remain fixed in a given location in the target tissue for an extended period. It should be noted that the number of fibres in a given mass can vary over at least two orders of magnitude depending on variations in the distribution of fibre size.

Width differences in the durability of man-made mineral fibres have been demonstrated both *in vivo* and *in vitro*, and depend on the chemical composition. The most durable man-made mineral fibres are also likely to be more hazardous to man than relatively soluble fibres. It would appear that, in order to predict health hazards from man-made mineral fibres, their dissolution rates in tissues would have to be determined for each fibre product. Other factors, such as surface properties and, for some man-made fibres, chemical leaching from fibres may also play a role, but these are much less well understood.

The precise mechanisms by which fibres exert a carcinogenic effect are unknown; however, in studies of experimental animals exposed to mineral fibres by inhalation in which significant tumour levels are seen, a high frequency of fibrosis is also usually found. A possible causal relationship has been suggested.

Present scientific knowledge indicates that the major determinants of the carcinogenic potential of fibres are biological durability, dimensions (length and diameter) and, as for any other carcinogen, dose to the targest organ. In this monograph, specific evidence is evaluated concerning the carcinogencity of glass fibre, rockwool, slagwool and ceramic fibres as groups. It is conceivable, however, that the fibre characteristics, durability and physical dimensions span the categories of all mineral fibres, including the man-made mineral fibres evaluated here, and that these are the characteristics that are most important in relation to the possible carcinogenicity of a material.

Considerations regarding epidemiological studies

In this monograph, standardized mortality ratios (SMRs) for lung cancer found in the cohorts differ depending on whether national or local reference comparisons were made. This is a potential problem in studying countries where lung cancer rates vary markedly from area to area, and particularly in the absence of extremely high SMRs. Intepretation of a study may be difficult if one of these ratios deviates significantly from unity while the other does not or deviates in the opposite direction.

Characteristics of the occupational cohort under study may suggest which type of ratio is more appropriate. For example, if a cohort has been assembled from a number of factories in various representative (rather than all urban) parts of a country, a nationally-based SMR may be more appropriate. The same might be the case if a particular factory has attracted a work force from representative areas of a country, including different ethnic groups. However, if a cohort has been drawn from only one factory with a locally-recruited work force, a locally-based SMR would be more appropriate. The population base from which the local rate is derived should be large enough that it is not dominated by the work force under study and that it permits (reasonably) stable estimates to be made. The latter requirement may not always be fulfilled for rare diseases, although statistical imprecision in the reference rates can be taken into account in the analysis. The presence of an increased risk caused by another local industrial exposure may also have considerable impact on local rates with regard to rare disorders; this situation would suggest that national (or regional) rates be applied.

Evaluation[1]

There is ***sufficient evidence*** for the carcinogenicity of glasswool and of ceramic fibres in experimental animals. There is ***limited evidence*** for the carcinogenicity of rock-

wool in experimental animals. There is *inadequate evidence* for the carcinogenicity of glass filaments and of slagwool in experimental animals. There is *inadequate evidence* for the carcinogenicity of glasswool and of glass filaments in humans. There is *limited evidence* for the carcinogenicity of rock/slagwool in humans. No data were available on the carcinogenicity of ceramic fibres to humans.

Overall evaluation[1]

Glasswool is *possibly carcinogenic to humans (Group 2B).*[1]

Glass filaments are *not classifiable as to their carcinogenicity to humans (Group 3).*[2]

Rockwool is *possibly carcinogenic to humans (Group 2B).*[1]

Slagwool is *possibly carcinogenic to humans (Group 2B)*[1]

Ceramic fibres are *possibly carcinogenic to humans (Group 2B).*[1]

Source: IARC Monographs on the Evaluation of Carcinogenic Risks of Chemicals to Humans: Man-made Mineral Fibres. Vol. 43, IARC, Lyon, France (1988).

II. Alcohol drinking

The forty-fourth volume of the IARC Monographs is a detailed study on alcohol drinking. It comprises six major sections: Alcohol Drinking and the Public Health; Worldwide Production and Use of Alcohol Beverages; Chemical Composition of Alcoholic Beverages; Additives and Contaminants; Biological Data Relevant to the Evaluation of Carcinogenic Risk to Humans; Epidemiological Studies of Cancer in Humans; it includes a summary of data reported and an evaluation.

The terms 'alcohol' and 'alcoholic beverages' tend to be used interchangeably to designate the product consumed, and the same practice has been followed in this monograph. A distinction is made, however, between alcohol or alcoholic beverages and the substance ethanol. This monograph covers only data relevant to the consumption of alcoholic beverages by humans: occupational exposures to ethanol and exposures other than by drinking were not considered.

Most human societies have made and used alcoholic beverages. The major exceptions, prior to contact with European cultures, were the Pacific Islanders and the indigenous populations of most of North America. The distillation of alcoholic beverages has a long tradition on the Eurasian continent, beginning in the Far East and moving to Europe via Arabia about a millenium ago. Traditional alcoholic beverages are fermentation products of a wide variety of organic materials, including grain (beer, *shochu*), fruit (wine, cider), sap (palm wine, pulque) and honey (mead). Since distillation was traditionally associated with pharmacy, many substances other than ethanol have often been included intentionally in distilled drinks. Thus, traditional alcoholic beverages and commercially produced beverages contain many constituents other than ethanol and water.

Alcoholic beverages have a wide variety of functions for humans. They quench thirst, in some parts of the world more hygienically than local water supplies; they are nutritional and, in some situations, can lead to excess caloric intake or an unbalanced diet. It has been estimated that alcohol may provide as much as one-quarter of the caloric intake of male agricultural workers in wine production areas. Alcohol has also been used medicinally in many cultures and is present as a solvent in pharmaceutical preparations.

Alcoholic beverages have diverse symbolic functions: alcohol is used in many religious observances; it is often associated with feasting and celebration; having or sharing a drink may be a ritual of solidarity or friendship, of sealing an agreement, of marking a rite of passage or of indicating that normal social constraints are suspended. In different cultures, various powers are attributed to drinking, and diverse behaviours are associated with drunkenness. In some societies, intoxication leads to and, to some extent, is used to explain disruptive or violent behaviour.

Abstaining from drinking has often had a sociocultural meaning. For Muslims, abstention is both a religious duty and a mark of differentiation from those of other faiths. In ancient China, abstention was expected of those holding government offices. In nineteenth century Britain, serious persons who wanted to better the lot of their children signed a pledge of abstinence.

In cultures where alcohol is valued, access to it has often been the prerogative of those of higher status. This may reflect a scarcity value, an ideology that intoxication is appropriate only for those of higher status, or fear that intoxication may produce insurrection. It is notable that the access of groups of persons who have been considered to be of socially subordinate status, such as women and children, has frequently been limited. However, according to WHO, abstinence among women has decreased dramatically in many countries, and, in a number of countries, young people have also increased their drinking.

In traditional societies, the availability of alcoholic beverages depended mainly on agricultural abundance and climate. In a tropical climate, production of alcoholic beverages may be a simple task, whereas in pre-industrial times, in regions such as Iceland, alcoholic beverages were all imported. Alcohol has long been an item of trade: the abundance of amphoras from the classical world testifies to the long-standing importance of wine in Mediterranean trade patterns. The spread of distilled beverages in the seventeenth and eighteenth centuries partly reflects their function as a form of agricultural surplus that did not spoil and was relatively transportable.

In traditional societies with no cash economy and poor transportation connections, fermented beverages were, and still are, consumed relatively quickly after their production, before spoiling. Such production is frequently seasonal—for example, at harvest time or on festive occasions—and is often associated with a culturally sanctioned drink-

[1] *Group 2.* The agent is possibly carcinogenic to humans.
This category is generally used for agents for which there is *limited evidence* in humans in the absence of *sufficient evidence* in experimental animals. It may also be used when there is *inadequate evidence* of carcinogenicity in humans or when human data are nonexistent but there is *sufficient evidence* of carcinogenicity in experimental animals. In some instances, an agent for which there is *inadequate evidence* or no data in humans but *limited evidence* of carcinogenicity in experimental animals together with supporting evidence from other relevant data may be placed in this group.

[2] *Group 3.* The agent is not classifiable as to its carcinogenicity to humans.

ing pattern or intermittent extreme intoxication, where all the alcoholic beverage produced for the occasion is rapidly consumed. In such circumstances, variations in agricultural supply can limit drinking.

Such traditional societies have gradually disappeared over the last few centuries as more peoples are incorporated into a global market economy. Groups moving from a traditional into an urban cash economy often preserve their drinking patterns initially, but engage in them more frequently. In general, the advent of industrially produced alcoholic beverages with an indefinite shelf-life, improvements in transportation and participation in a cash economy have erased constraints on availability of alcohol. Under these circumstances, constraints on consumption depend on State controls, on availability and price and, for example, on religious and social limitations.

With time, home-made and locally produced alcoholic beverages tend to be replaced by industrially produced alcohol. In the USA and the UK, industrially brewed beer replaced cider in the nineteenth century. Today, the process continues in countries such as Zambia and Mexico, as lager-style beer replaces opaque beer and pulque. The attractiveness of industrially produced alcoholic beverages is enhanced by the cosmopolitan, high-status connotations given to them by advertisers. Governments also have a fiscal interest in the industrialization of production, since it facilitates the collection of revenues based on drinking. Although the epidemiological evidence reviewed in this monograph is based primarily on commercially produced alcoholic beverages, it should be kept in mind that much of the world's alcohol consumption is of noncommercially produced alcoholic beverages.

Even in Europe, the current level of availability of alcoholic beverages is a relatively recent historical phenomenon. In the seventeenth and eighteenth centuries, spirits shifted from a pharmaceutical status to an item of everyday consumption, as industrial production methods flooded the market. Technological innovations transformed beer production, starting in the latter part of the nineteenth century, from a craft producing beverages for local and immediate consumption to an integrated industry producing a beverage that could be transported worldwide and stored almost indefinitely. Improvements in agricultural methods and the development of disease-resistance vines have allowed greatly increased wine production and consumption. Thus, wine consumption in France quadrupled in the last decades of the nineteenth century.

Effects of drinking

Alcohol consumption is associated with many health problems, which can be divided into three main types: chronic physical problems, casualty and disability problems, and mental problems.

According to WHO, physical health problems include, notably, cirrhosis of the liver, cancers at various sites, effects on the developing embryo and foetus, and other diseases affecting the gastrointestinal, cardiovascular, respiratory, nervous and reproductive systems. The relationship between alcohol intake and the occurrence of cardiovascular disease appears to be J-shaped, with the risk for abstainers being slightly higher than that in moderate drinkers (i.e., those consuming fewer than two or three drinks per day) and substantially lower than that for heavy drinkers. The reduced incidence of coronary heart disease may explain the lower total mortality among moderate drinkers which has often been found in relation to alcohol intake. Possible confounding effects of socioeconomic variables cannot be excluded in the light of their correlation with past alcohol consumption, and data with regard to women are limited.

Alcohol is causally implicated in many types of casualty, including road-traffic deaths, drownings, burns, falls, suicides and acute poisoning. Mental problems associated with drinking include a wide range of neurological consequences of prolonged heavy consumption, depression and other mental disorders. WHO notes that a prominent adverse consequence of drinking is the alcohol dependence syndrome, a term which encompasses both physical and psychological aspects of addiction to alcohol. The pharmacological basis of alcohol dependence has been reviewed also in this monograph.

WHO reports that although, at an individual level, alcohol consumption can be associated with domestic violence and neglect, and criminal behaviour and, at a collective level, can result in loss of production due to absenteeism and reduced efficiency, the drinking of alcoholic beverages is a source of pleasure and of solace to many people and facilitates human contacts in many societies.

In studying potential causal relations between alcohol consumption and health or social problems, it is important to consider and investigate the aspect of alcohol consumption that may be involved—total volume of ethanol consumption, frequency of bouts of drunkenness or length of time spent with the amount of blood-alcohol above a given level. Questions of exposure measurement in epidemiological studies are discussed in detail in this monograph.

Responding to alcohol-related problems

Efforts by society to reduce the toll of alcohol-related problems are cited in the earliest written records of mankind. Societies and ethnic groups in which there are now few alcohol-related problems reacted in different ways: for example, during several Chinese dynasties severe controls were enacted on drinking, while Israelite prophets preached against drunkenness and its consequences. The prohibitions on drinking in the Koran were proclaimed in response to a situation in Middle Eastern societies during the sixth century.

Until the late nineteenth century, governmental actions to reduce alcohol-related problems rarely took account of public health issues; authorities were more concerned with social disorders, destitution, vagrancy and vices, which were seen as being due to drinking. The role of drinking casualties did not become a matter of policy concern until the age of railways and automobiles, and the involvement of drinking in such specific disorders as cirrhosis and delirium tremens was clarified only in the nineteenth century. Although small groups of physicians actively pressed for temperance policies in a number of countries, the consequences of drinking usually played a small part in policy decisions during this period. As a reaction to prohibitionist claims, there was a tendency in the medical literature of the 1940s and 1950s in some countries to discount any chronic biological consequences of drinking; in the 1940s, a review of findings on the biological effects of drinking disclaimed any connection between drinking and cancer, and even questioned a direct relationship with cirrhosis.

Since the Second World War, public health considerations have taken priority in actions to combat alcohol-

related problems. Responding to the high prevalence of alcohol-related medical problems among their patients, French doctors led the way to some extent, with the concept of the 'alcoholization' of society. In other countries in the 1950s, actions to reduce the role of alcohol-related traffic casualties had been instituted. Otherwise, the responsibility of public health officials in the management of alcohol-related problems was limited to the provision of treatment for relatively marginalized populations of 'alcoholics', without regard to the general population of 'normal drinkers'. Arguments for instituting preventive activities oriented towards the long-term biological consequences of drinking are a relatively new phenomenon in many countries, although they have become widespread in recent years.

Increased interest in the chronic biological effects of drinking also reflects objective conditions: in most industrialized societies, alcohol consumption levels, after having reached a low in the 1930s, rose steeply in the period after the Second World War, resulting in substantial increases in mortality from cirrhosis and in other indicators of biological effects. In many countries, alcohol consumption levels have now stabilized, but at much higher levels than earlier in the century. In the meantime, the number of known chronic biological effects of alcohol has grown considerably, although dose-response curves are not well established. In particular, the importance of the pattern of drinking, as distinct from the overall volume of drinking, is not well understood for many conditions.

Societies have adopted various strategies to diminish alcohol-related problems. Some measures aim at reducing the consequences without necessarily affecting drinking patterns themselves; others aim at structuring drinking and associated behaviour in order to minimize harmful effects; and a third type aims at reducing the level of consumption, particularly heavy drinking. While the first two types of measure are important elements of an overall plan to tackle social and casualty problems, the third type is the most important with regard to chronic biological consequences.

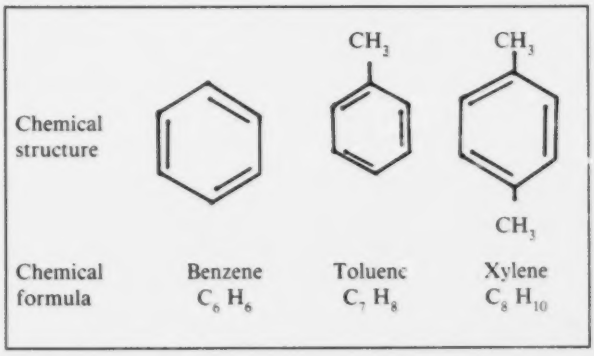
In most societies, there is some form of control to restrict the availability of alcohol. The State may monopolize the sale or production of alcohol, or may licence others to sell or produce on condition that they comply with licence requirements. Commonly, some limits are placed on the hours and conditions of sale. Investigation of the effectiveness of such actions suggests that it is limited unless the restrictions are very stringent. Price control, normally through excise taxes, has been used for a long time but is often motivated more by fiscal interest than by concern for the public health. Recently, there has been renewed interest in, and evidence of the effectiveness of, taxes as a constraint on consumption levels. Other controls that have proved effective include rationing the supply available to any one individual and setting minimum age levels below which drinking is not permitted. Control measures are most likely to be effective in the long term when popular support is substantial. Major reductions in the consumption level in a society tend to occur either in situations of social crisis, such as war, or in response to large-scale popular movements and shifts in consciousness concerning drinking.

Education and public persuasion campaigns have been a popular strategy for prevention in all societies concerned about the level of alcohol-related problems. WHO notes that such campaigns are unlikely to be strongly effective if they are pursued in isolation from other strategies. As with cigarette smoking, education and persuasion efforts are likely to be potentiated in periods of shift in popular sentiments concerning drinking. In the period after the Second World War, many industrial societies built up extensive alcoholism treatment systems, partly with the aim of reducing the rate of alcohol-related problems in the population. While such treatment is crucial, studies have shown that there is a substantial relapse rate after any type of treatment, suggesting that the provision of treatment and early case finding is only moderately effective in preventing future alcohol problems. It is in this context and because of growing popular opinion to reduce alcohol consumption in many countries that broader approaches to alcohol problems have come to the fore.

Source: IARC Monographs on the Evaluation of the Carcinogenic Risks of Chemicals to Humans: Alcohol Drinking. Vol. 44. IARC, Lyon, France (1988).

III. Environmental carcinogens—methods of analysis and exposure measurements

The series *Environmental Carcinogens: Methods of Analysis and Exposure Measurements* published by the International Agency for Research on Cancer (IARC) is designed to meet the need for methods of sampling and analysis of environmental carcinogens, both known and suspected, in the context of epidemiological and analytical studies. A major objective of the series in relation to the IARC is to provide a focus of past and present sampling and analytical procedures. This is necessary for a more reliable assessment of exposure. Volume 10 of the series deals with benzene, toluene and the xylenes.



Benzene has been assessed in two IARC Monographs (Volumes 7 and 29), as well as in IARC Monographs Supplement 7. Benzene, toluene and the xylenes are produced on a massive scale (in the millions of tonnes annually in many industrialized countries) and are employed in a great variety of applications as chemical intermediates, solvents and components in gasoline. They have often been employed together and it should be noted that commercial toluene can contain varying amounts of benzene. Toluene and xylenes are increasingly employed as 'safe' replacements for benzene in solvent applications. Major sources of these aromatic hydrocarbons in the environment are losses during production, transportation and processing of petroleum, refueling and operation of motor vehicles, and their use (particularly toluene and xylene) as solvents.

There is a broad potential for the exposure of industrial workers engaged in production and use of these agents as solvents and chemical intermediates (particularly in the rubber and plastics industry), and of the general public through dissipation into the environment, vehicle exhausts, consumer products, etc. Toluene and the xylenes are present in a wide range of commonly available household products, such as paint and varnish removers, rust removers, adhesives and glues. Toluene, moreover, has been widely abused by 'glue sniffers'.

Indoor concentrations of aromatic hydrocarbons, such as benzene, toluene and xylene, have often been found at levels which exceed those outdoors. The presence of benzene and toluene indoors arises primarily from tobacco smoke.

In order to furnish as comprehensive a treatment as possible, reviews concerning the epidemiology, use and occurrence, carcinogenicity, genetic toxicity, metabolism and pharmacokinetics of the title compounds are included in this volume. The importance of sampling and analytical techniques is stressed in six review chapters dealing with industrial, ambient and indoor air, chemical waste disposal sites, water and food and biological monitoring. Three analytical methods written in the International Organization for Standardization (ISO) format cover the determination of the designated aromatic hydrocarbons in industrial and ambient air, while seven procedures described for the determination of benzene, toluene and xylene in breath, and their metabolites in blood and urine, reflect the increasing recognition of the utility of biological monitoring in providing data related to recent or accumulated exposures.

The Editorial Board for this document continues to be aware of the need to recognize advances in the state-of-the-art and to incoporate procedures reflecting enhanced sampling proficiency, accuracy, sensitivity, specificity, reproducibility, ease of manipulation and, as far as possible, economy, particularly since analytical chemists and other scientists in developing countries may often find the facilities at their disposal to be less advanced than those available in more affluent societies.

Source: Environmental Carcinogens: Methods of Analysis and Exposure Measurements, Vol. 10: Benzene and Alkylated Benzenes, IARC, Lyon, France (1988).

International Programme on Chemical Safety

I. Environmental Health Criteria documents

The International Programme on Chemical Safety under the joint sponsorship of UNEP, ILO and WHO has published Environmental Health Criteria documents on: cypermethrin; dichlorvos; dithiocarbamates, ethylenethiourea and propylenethiourea; and pyrrolizidine alkaloids.

These documents are based on a comprehensive search of available original publications, scientific literature and reviews, and examine: the physical and chemical properties and analytical methods; sources of environmental and industrial exposure and environmental transport; chemobiokinetics and metabolism including absorption, distribution, transformation and elimination; short- and long-term effects on animals (carcinogenicity, mutagenicity, and teratogenicity); and finally an evaluation of risks for human health and the effects on the environment.

Summaries of these criteria documents are published in the section 'News about Chemicals' of this Bulletin.

II. Health and Safety Guides

The International Programme on Chemical Safety, under the sponsorship of UNEP, ILO and WHO is responsible for the publication of the series of Environmental Health Criteria documents, each of which assesses in detail the existing information on the relationship between exposure to a specific chemical, mixtures of chemicals, or a combination of chemicals and physical and biological agents, and human health and the integrity of the environment. The Environmental Health Criteria documents provide guidance for setting exposure limits consistent with the protection of human health and the environment.

In order to facilitate the application of these guidelines in national chemical safety programmes, IPCS decided to publish summaries of the criteria documents in the form of Health and Safety Guides. They highlight the information contained in the criteria documents for those who need to know the health and environmental issues involved, but not the scientific details. They also provide authoritative advice on accident prevention and protection of workers exposed to potentially toxic chemicals. The information is addressed to workers directly involved in the handling of chemicals, as well as administrators and managers responsible for chemical safety.

Each guide concentrates on a certain chemical, providing clear instructions for safe handling, storage, transport and disposal. Information ranges from protective clothing through to the exact medications to be kept in first-aid kits; it also lists the properties of the chemical that can create hazards of fire or explosion. Tables and charts suitable for reproduction as posters or safety cards are included. Each guide also outlines emergency medical treatments specific to the chemical and informs physicians of the symptoms to look for during periodic employee medical examinations. The concluding section of the guide provides a compact summary of current regulations, guidelines and standards governing exposure limit values, labelling, packaging, transport, and acceptable procedures for waste disposal. The guides also include general advice on other preventive and protective measures and emergency actions.

The 'Health and Safety Guides' so far published are:

1. Acrylonitrile
2. Kelevan
3. Methylene chloride
4. Tetrachloroethylene
5. Epichlorohydrin
6. 1-butanol
7. 2-butanol
8. *tert*-butanol
9. Isobutanol
10. Tetradifon
11. 2,4-dichlorophenoxyacetic acid (2,4-D)
12. Tecnazene
13. Chlordane
14. Heptachlor
15. Propylene oxide
16. Ethylene oxide
17. Endosulfan
18. Dichlorvos
19. Pentachlorophenol
20. Dimethoate
21. Aldrin/Dieldrin
22. Cypermethrin
23. Quintozene
24. Allethrins
25. Resmethrins
26. Pyrrolizidine alkaloids
30. Deltamethrin
31. Tetramethrin
32. d-Phenothrin
33. Permethrin
34. Fenvalerate

Copies of the 'Health and Safety Guides' are available on request from: Sales and Distribution Division, World Health Organization, CH-1211 Geneva 27, Switzerland.

International Maritime Organization

Recycling of oily waste in the marine industry

The International Maritime Organization (IMO) and the International Association of Independent Tanker Owners (INTERTANKO) have jointly published a report 'Recycling of Oily Waste in the Marine Industry'. It is an outcome of a study sponsored by both bodies. A summary and the conclusions of this report are outlined below.

In 1954 the International Convention for the Prevention of Pollution of the Sea by Oil was adopted to reduce oil pollution at sea by ships. This convention was eventually deposited with the IMO. Furthermore, the International Convention for Prevention of Marine Pollution from Ships adopted in 1973, as modified by the Protocol of 1978 (generally known as MARPOL 73/78) laid down the legislations and guidelines for the maritime industry. MARPOL 73/78 also contains a number of requirements for protecting the marine environment from oil pollution or oily waste being discharged into the sea. Countries that have ratified MARPOL 73/78 are under obligation to take positive actions in order to comply with these regulations.

Since then, considerable progress has been made, especially in the handling of oil-contaminated ballastwater onboard oil tankers and the installation of ballastwater reception facilities in larger oil handling ports and terminals. However, reception facilities are needed not only for oil tankers, but for all ships generating oily waste. In order to reduce or avoid oily waste being dumped at sea, ships are now required to retain waste on board for disposal in ports. Adequate facilities for the reception of such waste are therefore required in all ports receiving ships.

It is evident that a large number of ports throughout the world do not provide adequate arrangements for oily waste to be received from ships. This shortage of reception facilities has created a great dilemma for ship owners, as they may face large fines if found guilty of dumping or disposing of oily waste unlawfully at sea. Not only is this shortage of adequate reception facilities a breach of MARPOL 73/78 regulations (adopted by over fifty maritime countries world-wide), but also constitutes a serious environmental pollution problem, that now requires firm and urgent attention.

Ports visited by 500 to 2,000 seagoing vessels per year may expect quantities of oily waste for disposal amounting from 5,000 to 10,000 tonnes per year. Such quantities of oily waste may be sufficient to justify a waste oil regeneration plant to be operated on a commercial basis.

The report discusses the shortage of smaller reception facilities in ports and how to approach this problem, using small stationary or mobile reception tanks within the ports. These smaller units may be operated as a network, integrated with a centrally located waste oil refinery. Within such a concept, a business enterprise may be set up, which would be financially supporting its own activities.

The various disposal options for waste oils, in particular the technological possibilities of refining waste oils into fuel oil distillates and base oils (from which lubricating oils may be blended) are considered in the report. It notes that waste oils generated on board ships are often mixtures of fuel oils and are not suitable as feedstock for refining into lubricating oil. Commercial considerations for refining waste oils into fuel oils are discussed and an illustrative budget is provided for a hypothetical waste oil refinery. Quality requirements are given for waste oils suitable for recycling, refining into fuel oil and lubricating oils.

The report makes the following conclusions:

—Governments and environmental authorities should require port authorities and operators to clearly demonstrate how adequate reception facilities for oily waste are provided in their ports. Minimum capacity requirements and practical management procedures should be taken into account. The above authorities should, upon ascertaining that such facilities are adequate, certify their approval by an appropriate means. The adequacy of facilities should be reviewed periodically and certification renewed.

—Port authorities should provide such facilities free of charge to ships visiting ports for commercial purposes. Costs for the reception of oily waste should be included in the overall charges. For extra large quantities however, separate charges may be necessary to cover costs.

—Port authorities should liaise with local waste oil companies making sure they are capable and willing to receive oily waste in accordance with ships requirements and arrange disposal of oily waste in accordance with required environmental standards.

—The Oil Record Book, showing where oily waste has been discharged, should be regularly checked that waste oil/oily waste actually has been discharged in reception facilities and not at sea. For offences, penalties should be imposed.

—International regulations limiting the quantity of oil discharged from ships should be strictly enforced. This would further reduce oily waste being discharged at sea but also better make up quantities required for processing in ports. Discharge of oily waste in open sea is today permitted.

—Governments shall where possible exempt tax on oily waste in order to improve commercial feasibility for companies involved in the recycling industry and thereby support the environmental protection efforts.

Source: 'Recycling of Oily Waste in the Marine Industry.' International Maritime Organization, 4 Albert Embankment, London, SE1 7SR, UK (November 1988).

Commission of the European Communities

EUROTOXNET

The Commission of the European Communities (Health and Safety Directorate) is implementing a project to establish European Poison Information Network and Training Centres (EUROTOXNET). The aims of the EUROTOXNET are to develop a computerized system for on-line information exchange between European Poisons Centres, and national and international organizations concerned with health and poison prevention and to provide training in human toxicology and information technology.

The EUROTOXNET project will develop a common computer data base consisting of several inter-related files: *1. Cases of human poisoning.* All cases of poisoning reported to the participating Poisons Centres will be recorded in a standardized and harmonized format. It will provide immediate access to a much larger and more accurate

pool of evaluated case histories of poisoning and suspected poisoning than has previously been available. The information will be useful for the evaluation of human toxicity and treatment of poisoning, and for epidemiological studies to identify hazards and monitor prevention. Patient confidentiality will be maintained.

2. *Chemical substances.* Detailed toxicological information on chemical substances (particularly those used in pharmaceuticals, in industrial, agrochemical and household products and those occurring in natural toxins and as products of combustion) will be collected and evaluated with reference to acute and chronic poisoning in humans.

3. *Products.* Relevant information on composition, ingredients, physical hazards and labelling of commercial products will be recorded. Access to detailed formulation information will be restricted to respect manufacturers confidentiality requirements.

4. *Analytical methods.* Information on the type and location of analytical methods suitable for use in human samples and their interpretation.

5. *Bibliographic information.* A bibliography will support and be linked to the other four data bases through a special toxicology dictionary/thesaurus.

6. *Ancillary information.* Information on location of supplies of antidotes and specialist laboratories, and on names and addresses of toxicologists and other experts.

The fundamental role of Poisons Centres is to provide an immediately available 24-hour, expert information and advice service for any case of poisoning or suspected poisoning. Poisons Centres are the focal point of Poisons Control Programmes, which are concerned with diagnosis and treatment of poisoned patients and with identification of risks of poisoning in the local population, in order to establish preventive measures.

EUROTOXNET will assist Poisons Centres staff answering telephone enquiries about the management of cases of human poisoning, identify the substances involved, and find out about the effects and treatment. They will also be able to enter details of the enquiries into the computer, on-line, while they are talking to the enquirer.

The data bases in each centre will be linked by a telecommunications network, so that non-confidential information about commercial products and cases of poisoning registered at one Poisons Centre, will be available to all Centres on the network. Other organizations will be able to link into this network. EUROTOXNET will also improve the speed and quality of communication in an emergency, such as a major disaster involving chemicals, and also alert all Poisons Centres, Government Departments, manufacturers and Customs Officials.

EUROTOXNET is being developed in three phases:

Phase 1: the system will be piloted, developed and installed in the Poisons Centres in London, Brussels and Milan, and communications links established between them. This was expected to take three years, and will be completed by the end of 1990.

Phase 2: the system will be installed in other UK and European Poisons Centres when they join the project.

Phase 3: an expert system with confidentiality controls will be developed so that EUROTOXNET can be used in UK and European hospitals, government agencies and manufacturers, both for input and retrieval of information.

EUROTOXNET will give training in the use of the computerized information retrieval systems and in human toxicology.

Training will be given mainly through working with the team developing the EUROTOXNET computer data base. Trainees will work on projects concerned with the collection and evaluation of data or with the design of the database which use the ORACLE Relational data base software, operating on UNIX platforms.

The training programme is aimed at medical doctors and other professionals such as pharmacists, information scientists and nurses, who may have had experience of working in poisons centres, hospitals and general practices. However people working in toxicology or in related fields such as product safety, for government or industry, or students on postgraduate courses in toxicology or information science will be eligible to be considered for training and will be encouraged to participate in the programme. In the first three years, up to the end of 1990, the EUROTOXNET centre in London will train at least 20 people. In addition, it may be possible to train staff from other organizations, subject to negotiation.

More information about the EUROTOXNET Project and Training Programme can be obtained from: Dr. V. Murray, UK Director of EUROTOXNET, Poisons Unit, Avonley Road, London SE14 5ER, United Kingdom.

Conservation of Clean Air and Water—Europe

The oil industry organization, Conservation of Clean Air and Water—Europe (CONCAWE), has published a report entitled 'Health Risk of Exposure to Non-Occupational Sources of Benzene'. It gives a summary of the health effects of benzene. It also reviews the various risk estimates which have been published on the likelihood of an increase in incidence of leukaemia in the general population as a consequence of benzene in the ambient air. It also identifies the sources of benzene exposure for the general population. The following is a summary of this report.

Repeated exposure to high concentrations of benzene vapour is associated with the occurrence of leukaemia. On this account, benzene is classified as a human carcinogen. However, no case of benzene-induced leukaemia has been confirmed following regular and repeated exposure at work to benzene at concentrations below 100 ppm (320 mg/m^3). Benzene also causes depression of blood formation, but again no case of benzene-induced depression of blood formation has been confirmed at concentrations below 25 to 30 ppm (80 to 96 mg/m^3). Benzene causes chromosomal aberration, but there is no evidence to link these with the occurrence of leukaemia.

A maximum permissible time weighted average workplace exposure for benzene of 5 ppm (16 mg/m^3) and an action level of 1.5 ppm (4.8 mg/m^3) has been proposed in the ECE.

The main routes of benzene exposure are by inhalation and by ingestion from the diet. Only about 50% of inhaled benzene is absorbed and converted to toxic metabolites. No human data are available on the metabolic pathway or rate of excretion of ingested benzene.

The principal sources of benzene exposure for the general public are from diet, smoking and ambient air (natural and man-made emissions). Typical levels of benzene in ambient

air range between 1 ppb (3.2 $\mu g/m^3$) for rural areas and 6 ppb for industrial zones, although large excursions around these levels occur. It is estimated that a non-smoking, non-occupationally exposed individual will have a daily benzene intake of up to 540 μg. Of this, diet accounts for about 250 μg. Inhaling the smoke of 20 cigarettes/day will add at least another 300 μg to the daily total. Thus, diet plus smoking can contribute 65% or more of the daily intake. A worker exposed to 1,500 ppb of benzene at work for 8 hours/day will add about 19,200 μg to the daily total, an increment of some 23 times greater than the daily intake of a smoking member of the public living in an industrial neighbourhood.

Various assessments of the risk for the general population developing leukaemia as a result of exposure to benzene in the ambient air have been made using dose-response data obtained from epidemiological studies on workers exposed to high concentrations of benzene. These assessments depend on a number of controversial assumptions which, combined with uncertainties about the exposure data, a failure to take account of biological/metabolic factors, and the wide variations in results of calculating the number of excess leukaemia cases per million population exposed to 1 $\mu g/m^3$ of benzene for a 70-year lifetime, raise considerable doubts about the value of such figures as realistic estimates of possible health risks.

Source: 'Health Risk of Exposure to Non-Occupational Sources of Benzene.' CONCAWE Report No 8/89. The Hague, Netherlands (September 1989).

United States of America

Reduction of hazardous waste

The United States Congress in November 1984 declared 'it to be the national policy of the United States that, wherever feasible, the generation of hazardous waste is to be reduced or eliminated as expeditiously as possible. Waste nevertheless generated should be treated, stored, or disposed of so as to minimize the present and future threat to human health and the environment'. In 1985, the hazardous waste report 'Superfund Strategy' (prepared by the United States Congress, Office of Technology Assessment (OTA)), examined the USA programme to clean up uncontrolled hazardous waste sites. The report was an effort to shed new light on the scope of the problem and showed how—for environmental and economic reasons—permanently effective cleanup techniques based on waste treatment can replace leaving or disposing Superfund wastes in the ground.

In 1986 the Congress turned its attention to preventing hazardous waste problems by cutting down on the generation of hazardous waste at its source through innovative engineering and management. The OTA later published its report 'Serious Reduction of Hazardous Waste' which examines what is meant by hazardous waste, waste reduction, and even waste reduction technology. The report also explores the meaning and consequences of giving primacy to waste reduction over waste management, and puts waste reduction squarely into the context of industrial production and efficiency, recognizing the constraints on the national economy. The following is a summary of this report.[1]

Waste reduction is an economically sensible response to what many people see as a hazardous waste crisis. Several millions of tonnes of hazardous waste generated annually from industrial operations enter all environmental media even though they may be within permitted or licenced limits. Many thousands of people have lost their drinking water sources because of contamination by toxic waste. Across the United States there are thousands of waste disposal sites contaminated by hazardous waste that require cleanup. An increasing number of lawsuits are being brought by people claiming to have suffered adverse health effects from living near toxic waste sites.

Waste reduction is critical to the prevention of future hazardous waste problems. Current pollution control methods often do little more than convert or move waste around. For example, air and water pollution control devices typically generate solid, hazardous waste that goes to landfills and too often leaches from there into groundwater. Therefore, the OTA finds that establishing a comprehensive, multimedia approach to reducing wastes going into the air, land, and water is essential.

Reducing wastes in an industrial process requires intimate knowledge of all aspects of that specific production process, in contrast to waste treatment, which is essentially an addition to the end of the process. However, there are five approaches that industry can take to reduce hazardous waste:

(i) change the raw materials of production,
(ii) change production technology and equipment,
(iii) improve production operations and standards,
(iv) recycle waste within the plant,
(v) redesign or reformulate end-products.

Among the opportunities that exist for common processing of wastes are:

(i) using mechanical techniques rather than toxic organic solvents to clean metal surfaces,
(ii) using water-based raw materials instead of materials based on organic solvents and,
(iii) changing plant practices to generate less hazardous wastewater.

Moreover, waste reduction succeeds when it is part of the everyday consciousness of all workers and managers involved with production—where the reduction opportunities are, rather than when it is a job only for those responsible for complying with environmental regulations. A few people with end-of-pipe, pollution control jobs are not in a position to reduce waste by themselves; such efforts must involve upstream workers and facilities.

Source: 'Serious Reduction of Hazardous Waste.' Office of Technology Assessment, Congress of the United States, Washington D.C., 20510, USA (1986).

[1] Readers will find in Section III, 'News about Chemicals', a selected example given in the report on the possibilities for the reduction of hazardous waste resulting from the manufacture of acrylonitrite.

III. News about Chemicals

Acrylonitrile

This article has been extracted from a report published by the Office of Technology Assessment, Congress of the United States, entitled 'Serious Reductions of Hazardous Waste', which has been reviewed in Section II (page 19).

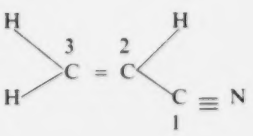
Identity

Common name: Acrylonitrile

Synonyms and trade names: Acrylon; acrylonitrile monomer; AN; Carbacryl; cyanoethylene; ENT 54; Fumigrain; Miller's fumigrain; 2-propenenitrile; TL 314; VCN; Ventox; vinyl cyanide

Molecular formula: C_3H_3N

Chemical structure:



Registry numbers: CAS 107-13-1
RTECS AT 5250000

Conversion factor:
1 mg/m³ = 0.4605ppm
1 ppm acrylonitrile = 2.17 mg/m³ at 25 °C and 101.3 kPa (760 mm Hg)

Properties, production and use

Acrylonitrile is a volatile colourless liquid, with a sweet, pungent odour. It has a melting point of −83.55 °C and a boiling point of 77 °C. It readily dissolves in water (73.5 g/litre − 20 °C). Other characteristics: it reacts violently with strong oxidizers, strong acids and basis; it decomposes in a fire, releasing harmful gases.

Technical acrylonitrile is more than 99% pure. It is stabilized against self-polymerization and yellow colour formation by the addition of hydroquinone monomethyl ether (35-50 mg/kg) and water (0.25-0.45%). The current production of acylonitrile is based on catalytic ammoxidation of propylene in the vapour phase. Bismuth phosphomolybdate is the most frequently used catalyst. The chief by-products are acetonitrile and hydrogen cyanide.

Acrylonitrile is mainly used in the production of synthetic fibres, resins, and rubbers, and as a chemical intermediate. It is also used in fumigants.

In 1985, acrylonitrile ranked 38th in the list of the top 50 chemicals made in the United States, ranked 20th out of the 26 organics on the list, and had the highest growth rate of the organics from 1975 to 1985 with an annual average growth rate of 6.8%. Production in 1988 was 2.576 billion pounds (1.1 million metric tons). For each metric ton of acrylonitrile product manufactured, 2.3 metric tons of process water and 400 metric tons of cooling water are used.

A description of the production processes and possibilities existing for waste reduction during the industrial manufacture of acrylonitrile is given below.

Process water

Water is used primarily as a quench neutralizer to cool the reactor effluent and neutralize any unreacted ammonia. Sulphuric acid is added to process water, and the acid solution is added directly to the quench neutralizer tower to effect very rapid cooling. Effluent from the quench tower is aqueous waste, essentially an ammonium sulphate solution. Based on the production rate of acrylonitrile, an estimated 2.5 million metric tons of process waste water is generated annually. This is roughly 1% of the national hazardous waste stream. The disposal cost of the waste water is estimated at $30 to $60 per metric ton of product based on using deep-well injection for waste disposal; the product cost is estimated at $560 per metric ton.

Possibilities for waste reduction. A process technology change is difficult because the process water serves two purposes: it cools the reactor effluent and serves as the medium for neutralizing the excess ammonia. Indirect cooling via a heat exchanger would probably not be rapid enough to replace the direct quench, and use of a heat exchanger surface might lead to the formation of tars or other undesirable sides reactions. Moreover, indirect cooling would not accomplish neutralization of the excess ammonia. To change the acrylonitrile manufacturing process to eliminate or reduce process waste water would constitute a major change. A large research effort might be required with a pilot and demonstration project and might take from 5 to 10 years at a considerable cost. Since the cost of the process waste water is only 5-10% of the total production costs, such an effort is not attractive. If waste water management costs were significantly higher, say two or three times more (from $60 to $180 per ton of product), then the effort might be justified—perhaps because of shifting from injection wells to treatment.

Cooling water

For every gallon of cooling tower water circulated, a small fraction called blow-down is discarded to remove the build-up of slime and solids which accumulate during recirculation. This blow-down contains toxic chemicals used as bactericides and fungicides and is a hazardous waste. A typical blow-down ratio is about 0.5% of the circulation rate. For each 400 metric tons of acrylonitrile about 2.2 million metric tons of this waste water is generated annually. Disposal cost of the waste water ranges from about $26 to about $52 per metric ton of product, or 5-10% of the product costs.

Possibilities for waste reduction. Here the water serves only one function, cooling. An alternative could be the use of a heat-pump cycle to reject heat to the environment from

a closed-loop coolant refrigeration system. After the use of the coolant to cool the process, it would be compressed to a higher temperature and pressure and then passed through a radiator that would reject the heat to the environment. The operating costs for cooling would be from $17 to $60 per metric ton of product. The costs for managing the traditional cooling waste water—if injection well costs are from $0.05 to $0.10 per gallon—would be from $26 to $52 per hour per ton of product (this cost could increase if a waste management shift occurred from deep-well injection to waste treatment). There is a clear potential for saving perhaps $20 per ton of product if an efficient, closed-loop, refrigeration were used instead of conventional water cooling. For a 100,000 ton per year plant this means a saving of about $2 million annually. Assuming that the capital costs of the refrigeration system might be at most about 10% of the original capital costs of the plant ($50 million), then payback would occur in a few years.

Sources: 1. 'Serious Reduction of Hazardous Waste.' Office of Technology Assessment, Congress of the United States, Washington D.C., 20510, USA, (1986).

2. 'Environmental Health Criteria 28: Acrylonitrile.' International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland (1983).

3. 'Health and Safety Guide: Acrylonitrile.' International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland, (1986).

Asbestos

Previous issues of the *IRPTC Bulletin* (Vol. 5 Nos. 1 & 3; Vol. 6 Nos. 2 & 3; Vol. 7 Nos. 2 & 3, and Vol. 9 No. 1) have reported on the effects of asbestos on human health and the environment. These have dealt mainly with control limits, measurements of airborne dust concentrations and assessment of control measures taken by various countries and the international organizations. The National Institute of Public Health and Environment Protection of The Netherlands has recently published in English the report 'Integrated Criteria Document Asbestos' (the original version in Dutch was published in November 1987). The following is a summary of the report.

The document contains data on asbestos relating to the sources and distribution pattern (soil, water, air), the risks to man in particular at current exposure levels, and the technical possibilities and economic consequences of reducing these risks. This information provided the scientific basis for the formulation of the effect-directed standardization policy of The Netherlands. Since the risks remain confined to exposure via the respiratory route, the emphasis is specifically on the environmental compartment air.

Asbestos is the generic name used for a family of fine inorganic fibres (mineral silicates), which can be classified either as serpentine (chrysotile) or amphibole (the other commercial asbestos type). Because of its thermal stability and chemical resistance, its electrical insulating property and high tensile strength, asbestos had a wide range of applications in the past. As a result of the now-known drawbacks of asbestos and the consequent regulations, the number of uses and the total consumption in The Netherlands have fallen sharply in recent years. Chrysotile is the only asbestos variety still processed in The Netherlands.

The form in which asbestos is released differs from one environmental compartment to another. Emission into the soil occurs chiefly from the dumping of waste products; soil contamination as a result of deposition and infiltration is relatively small. It concerns an annual total of about 4500 tonnes (in 1982), divided between bound (52%) and unbound (13%) asbestos and asbestos as a fraction of a very large waste stream (35%).

The emission into surface water was over 2.7 tonnes in 1982; this has since been cut back to 1.4 tonnes.

In 1982, about 2.3 tonnes were emitted into the air in The Netherlands, consisting for the most part of free asbestos fibres. In addition to a number of localized sources, there are significant diffuse sources. The principal emissions are caused by brake dust on roads (26%), processing of asbestos cement on site (20%), the manufacture of braking and friction materials (13%), the demolition of buildings and rubble breaking (12%), and brake dust in garages (16%). It is expected that these emissions will have risen by about 50% by the year 2000. The reasons for this are: (a) the presence of more asbestos in buildings that are due for renovation or demolition in the coming decades, and (b) the growth in road traffic.

Chrysotile is the principal asbestos type involved in these emissions; other asbestos varieties can only be of local importance. Re-emissions of fibres can contribute significantly to the asbestos load in the air; asbestos fibres are relatively inert and can consequently circulate in the environment for long periods of time. However, the extent of the contribution of re-emissions cannot be estimated at present.

Asbestos is the subject of much attention especially because of its effects on the health of man. The principal effect is the development of bronchial carcinomas (lung cancer) and mesotheliomas (tumours of the pleura and peritoneum) following exposure via the respiratory route. There is no evidence of a carcinogenic effect following exposure via the gastrointestinal tract. It is assumed that the current exposure level via the oral route involves a negligible risk.

The carcinogenic activity of asbestos at exposure via the respiratory route depends on the shape of the fibres (length/diameter ratio of at least 3), and especially on their dimensions. The critical fraction encompasses all respirable chrysotile and amphibole fibres with a length of more than 5 μm and a diameter of less than 3 μm, the most dangerous being fibres with a diameter of around 0.1-0.2 μm. As regards the development of mesotheliomas, the durability of the fibres in the body is also relevant. In this connection, chrysotile, which dissolves slowly in the lung tissue, seems to be less hazardous than the amphiboles.

The optical microscope measuring methodology, which is in routine use, is not satisfactory for the detection of fibres with the above-mentioned dimensions. For this electron microscope analysis techniques must be used. There is an urgent need here for a standardized method of assessing environmental samples.

In view of the carcinogenic properties of asbestos after inhalation, exposure via the respiratory route should be avoided as far as possible. There are no quality requirements for the outdoor air in The Netherlands. To make a risk estimate for the purpose of possible future standards for the environment, the WHO guideline was used, with a modification regarding chrysotile asbestos. The WHO

guideline is based on extrapolation of data from occupationally exposed individuals to the general population with an estimated 30% smokers (smoking increases the risk of lung cancer from exposure to asbestos). The estimated approximate risks to the general population at lifetime exposure to asbestos, measured as described above, indicate that exposure to chrysotile is associated with an excess of lung cancer, whereas the amphiboles cause an increased risk of developing mesotheliomas.

A lifetime risk of 10^{-6} (one excess death from mesotheliomas or cancer of the lung per 1,000,000 total deaths) will be caused by lifelong exposure to an estimated 10 to 100 amphibole fibres per m^3 (mesotheliomas), and by lifelong exposure to an estimated 100 to 1000 chrysotile fibres per m^3 (lung cancer in a population with 30% smokers).

Comparison of the exposure levels in the ambient air with this toxicological risk estimate shows that the expected lifetime risk of lung cancer in the immediate vicinity of asbestos sources and in a number of large cities and industrial areas is higher than 10^{-6}. In one area where amphibole asbestos was detected in the ambient air, the expected lifetime risk of mesotheliomas is also higher than 10^{-6}. The expected risks across The Netherlands remain below 10^{-4} (10^{-6} per year), which the Indicative Multi-year Programme (IMP) IMP-Environmental Management 1986-1990 considers to be the maximum allowable risk.[1] It is not known to what extent this maximum allowable risk is exceeded in the immediate vicinity of the numerous diffuse sources (garages, waste disposal sites, and the like).

Risk groups which may be exposed to high asbestos levels are (in addition to the workers in the asbestos-manufacturing and -processing industries) persons who, by virtue of their profession, spend long periods of time in public buildings and offices where sprayed asbestos has been applied, and demolition workers. Heavy physical exertion increases the respiration rate and thereby the exposure dose. Smokers constitute a risk group with an increased susceptibility to lung cancer.

In the case of an autonomous development, the emission into the air will increase in the near future. This increase is expected as a consequence of the presence of more asbestos in buildings that are due for renovation or demolition (a factor of 3 higher by the year 2000) and the growth in road traffic (50% higher emission by 2000 due to an increase in brake dust). There is the possibility that, if measures are not taken, the limits of the maximum allowable lifetime risks established by the standardization policy will be exceeded within a few decades. Measures aimed at controlling the emission of asbestos during all stages of the life cycle of asbestos-containing materials are therefore advisable. As regards the emissions during demolition and renovation activities, these can be reduced by about 90% at an annual cost of f5500 (f30 per kg asbestos emission avoided). To reduce asbestos emissions from braking and friction materials, it seems desirable that the use of substitutes be encouraged. However, it should be borne in mind that alternative materials may have a similar biological effect to asbestos. This should be evaluated for each material and application area.

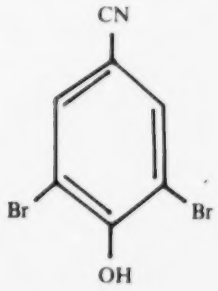
Source: 'Integrated Criteria Document: Asbestos.' National Institute of Public Health and Environmental Protection, Antonie Van Leeuwenhoeklaan 9, P.O. Box 1, 3720 BA/Bilthoven, The Netherlands (May 1989).

[1] The effect-directed standardization policy, as laid down in the Indicative Multi-year Programme (IMP)-Environmental Management 1986-1990, considers a lifetime risk of 10^{-6}, corresponding to 1 in 10^8 cases per year, to be the so-called negligibility level. This policy considers a lifetime risk of 10^{-4} corresponding to 1 in 10^6 cases per year, to be the maximum allowable risk. This risk is caused by lifelong exposure to an estimated 1000-10,000 amphibole fibres per m^3 (mesotheliomas), and an estimated 10,000-100,000 chrysotile fibres per m^3 (lung cancer in a population with 30% smokers).

Bromoxynil

The United States Environmental Protection Agency (EPA)[1] recently notified foreign governments, through the Department of State, of its regulatory action on the use of restrictions placed on the herbicide bromoxynil and also the cancellation and recall of certain bromoxynil formulations by the United States registrant. The following notice briefly describes the Agency's concern and evaluation of available scientific data and summarizes its conclusion to put restrictions on the use of bromoxynil.

Identity

Common name:		Bromoxynil
Chemical names:	IUPAC	3,5-dibromo-4-hydroxybenzonitrile
	CAS	3,5-dibromo-4-hydroxyphenyl cyanide
Synonyms and trade names:		Brittox; Brominal; Brominex; Brominil; bromoxynil; Broxynil; Buctril; Buctril Industrial; Butichlorofos; Chipco Brab-Kleen; Chipco Buctril; 2-6-disbromo-4-cyanophenol; Ent 20852; 4-hydroxy-3-5-dibromobenzonitrile; MB 10064; M&B 10,064; ME4 Brominal; Nu-Lawn Weeder; Ocytril M.
Chemical structure:		
Molecular formula:		$C_7H_3Br_2NO$
Registry numbers:	CAS	1689-84-5
	RTECS	DI 3150000

[1] Under Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), EPA has the responsibility for ensuring that pesticides do not cause unreasonable adverse effects to the public and the environment. Whenever the Administrator of EPA determines that continued sale, distribution or use of a pesticide poses a certain hazard to public health, he may take a number of actions: emergency suspension; notice of intent to cancel; or requirement for restrictions to reduce risk.

Properties and use

Bromoxynil is a colourless solid herbicide. It has a melting point of 194-195 °C and is slightly soluble in water (0.13 g/l at 20-25 °C). It is soluble in xylene, ethanol, n-propanol and many other organic solvents.

Bromoxynil is a post-emergence herbicide used to control broadleaf weeds in field corn, small grains (including wheat) and other crops such as garlic, onions, flax, mint and Canary grass.

Basis for concern

EPA's review of available bromoxynil data raised concerns about the potential developmental toxicity of bromoxynil. The agency was particularly concerned about the unborn foetuses of persons exposed to bromoxynil during mixing and loading operations and when applying the pesticide.

These concerns are currently based on an evaluation of development toxicity studies on bromoxynil that were conducted primarily with bromoxynil phenol. (The majority of the USA pesticides market consists of products formulated with bromoxynil octanoate.)

Most of the studies evaluated toxicity by the oral route of exposure rather than dermal exposure. EPA's evaluation of the available data focused primarily on the dermal route of exposure and accounted for differences in the rate of absorption for bromoxynil phenol and bromoxynil octanoate.

These studies indicate that bromoxynil causes developmental effects in both rats and rabbits. Specifically, supernumerary (extra) ribs were observed in dermal studies. Based on the studies and the estimated exposure for mixers, loaders and applicators of bromoxynil, EPA found that persons handling the pesticide could be potentially at risk.

EPA is not currently concerned about the dietary risk of bromoxynil because of the virtually non-existent dietary exposure to bromoxynil in the USA. Bromoxynil has not generally been detected on crops or in animal feed or forage.

Action being taken

On 9 May 1989 EPA announced the implementation of risk-reduction measures designed to protect workers handling bromoxynil during the imminent use season: bromoxynil may only be applied by certified pesticide applicators. The label will include a warning that pregnant women should avoid contact with the product because of the developmental effects observed in the offspring of laboratory animals exposed to the pesticide. Coveralls, over a long-sleeve shirt and long pants, as well as clean gloves and chemical-resistant shoes are to be worn when handling bromoxynil. Mixers/loaders are required to wear a chemical apron if using an open pour system. Ground boom applications on 180 acres or more per day must be carried out in an enclosed cab. If 30 gallons or more of bromoxynil products are to be used per day, a mechanical transfer system is required for mixing and loading operations.

In addition, the United States registrant, has announced a number of voluntary measures including: the voluntary cancellation and recall of all products containing bromoxynil butyrate which is more readily absorbed into the skin than bromoxynil octanoate. The registrant has made a number of package design changes to minimize mixer/loader exposure.

Future actions

The registrant is to generate a number of studies designed to allow a more accurate assessment of the exposure risks to bromoxynil. These include a dermal developmental toxicity study using bromoxynil octanoate in the rabbit, an expanded dominant lethal study in the rat to determine whether bromoxynil causes male reproductive toxicity effects, and a worker exposure study designed to assess exposure to users when employing various risk reduction measures.

The new data are required to be submitted in 1990. Thus, EPA expects to review the data before the 1991 growing season.

Source: Permanent Representative of the United States of America to the United Nations Environment Programme, P.O. Box 30137, Nairobi, Kenya (June 1989).

Chlorofluorocarbons

On 1 January 1989, the Montreal Protocol—the world's first regulatory agreement to protect the ozone layer—came into force. Twenty-nine countries and the European Community have now ratified the accord negotiated in September 1987 under the auspices of the United Nations Environment Programme, which has played such a major role in the development of an international agreement on the use of chlorofluorocarbons (see Bulletins Vol. 5 Nos. 1 and 3, Vol. 7 No. 4, and Vol. 9 Nos. 1 and 2).

Governments first committed themselves to preventing assaults on the ozone layer at a March 1985 conference, from which emerged the Vienna Convention for the Protection of the Ozone Layer. The Montreal Protocol's regulatory measures follow up on the Convention's general outline of the need to adopt measures to protect the ozone layer. The accord could only come into effect if those countries which ratified it together accounted for at least two-thirds of the global consumption of ozone-depleting chemicals, currently about 1.14 million tonnes per year.

The parties to the Protocol, most of them industrialized countries, currently consume about 80% of these chemicals. The United States and the European Community together consume 60%. Other major consumers are Japan, 12%, and the Soviet Union, about 9%.

Principal among the culprit chemicals are fully halogenated chlorofluorocarbons (CFCs), used in refrigeration, air conditioning, solvents in the electronics industry, foam insulation, packaging, and as aerosol propellants. Halons, key chemicals used in fire extinguishers, are also addressed in the accord.

The agreement freezes production of the five most destructive CFCs at 1986 levels, later reducing CFC consumption and production by mid-1998 in two stages: a 20% cut by mid-1993 and a further 30% reduction by mid-1998. The three halons will be frozen at 1986 levels.

However, in Sweden, the manufacture and import of aerosol containers using chlorofluorocarbons (CFC, freons) as a propelling agent has been prohibited as from 31 December 1988. The Swedish National Board of Health and Welfare may exempt aerosol preparations for medical use after consultation with the Swedish National Chemicals Inspectorate.

In the pharmaceutical manufacture of certain drugs, freons are most frequently used as propellants in aerosols intended for nasal application or inhalation. They are also used in some preparations of glyceryl trinitrate, in certain veterinary medicinal products and in products for external application. In most cases, it is considered that satisfactory alternative delivery systems can be devised, including powders for inhalation or mechanically-driven sprays. Special consideration will, however, be accorded to preparations intended for asthmatics in whom these alternative formulations may sometimes be less effective and less acceptable.

Sources: 1. *WHO Drug Information*. Vol. 2, No. 4. World Health Organization, CH-1211 Geneva 27, Switzerland (1988).
2. *Information från Socialstyrelsens Läkemedelsavdelning*. 13:151 (1988).

Cypermethrin

The International Programme on Chemical Safety has published an Environmental Health Criteria document on cypermethrin. An International Task Group discussed and finalized the document at a meeting held in Geneva. In addition, IPCS has published a Health and Safety Guide (HSG) on cypermethrin. A summary of the findings of the Task Group which discussed the criteria document is given below with the Conclusions of the HSG.

Identity

Common name: Cypermethrin

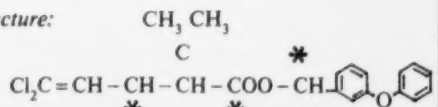
Chemical names:

IUPAC: (RS)-alpha-cyano-3-phenoxybenzyl (1RS)-*cis*-,*trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylate

CAS: (RS)-cyano(3-phenoxyphenyl) methyl(1RS)-*cis*-*trans*-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylate

Synonyms and trade names: Ammo; Avicade; Barricade; CCN 52; CG-A 55186; Cymbush; Folcord; Imperator; Kafil Super; NRDC 149; Polytrin; PP 383; Ripcord; Stockade; WL43467

Chemical structure:



Molecular formula: $C_{22}H_{19}O_3NCl_2$

Registry numbers: CAS 52315-07-8 (formerly 69865-47-0)

RTECS GZ 1250000

Properties and use

Cypermethrin is the ISO name for the pure racemic compound. The technical products commonly available contain more than 90% cypermethrin and the ratio of *cis*- to *trans*-isomers varies from 50:50 to 40:60. The data presented in this document refers to products within this range of composition, unless otherwise stated. In the chemical formula the asymmetric centres are marked with an asterisk and give rise to 8 isomers.

Some Physical and Chemical Properties of Cypermethrin

Physical state	varies from a viscous yellow liquid to a semi-solid crystalline mass at ambient temperatures
Relative molecular mass	416.3
Melting point	up to 80°C depending on purity and *cis:trans* ratio
Boiling point	decomposes at 220°C
Density (22°C)	1.12 g/ml
Solubility in water (20°C)	0.009 mg/litre
Solubility in organic solvents: hexane	103 g/litre
xylene	>450 g/litre
	also comparable solubility in cyclohexanone, ethanol, acetone, and chloroform
Vapour pressure (20°C)	1.9×10^{-7} Pa (1.4×10^{-9} mmHg)
n-octanol/water partition coefficient	2×10^6 (log P_{ow} 6.3)

Cypermethrin is highly stable to light and at temperatures below 220 °C. It is more resistant to acidic than to alkaline media, with an optimum stability at pH 4. Cypermethrin is hydrolysed under alkaline conditions in the same way as simple aliphatic esters: the rate-determining step is the nucleo-philic attack by a hydroxyl group. Dilute aqueous solutions are subject to photolysis, which occurs at a moderate rate.

Cypermethrin was initially synthesized in 1974 and first marketed in 1977 as a highly active synthetic pyrethroid insecticide, effective against a wide range of pests in agriculture, public health, and animal husbandry. In agriculture, its main use is against foliage pests and certain surface soil pests, such as cutworms, but because of its rapid breakdown in soil, it is not recommended for use against soilborne pests below the surface.

In 1980, 92.5% of all the cypermethrin produced in the world was used on cotton; in 1982, world production was 340 tonnes of the active material. It is mainly used in the form of an emulsifiable concentrate, but ultra low volume concentrates, wettable powders, and combined formulations with other pesticides are also available.

Chemically, cypermethrin is the alpha-cyano-3-phenoxybenzyl ester of the dichloro analogue of chrysanthemic acid, 2,2-dimethyl-3-(2,2-dichlorovinyl) cyclopropanecarboxylic acid. The molecule embodies three chiral centres, two in the cyclopropane ring and one on the alpha cyano carbon. These isomers are commonly grouped into four *cis*- and four *trans*-isomers, the *cis*-group being the more powerful insecticide. Cypermethrin is the racemic mixture of all eight isomers and, in this appraisal, cypermethrin refers exclusively to the racemic mixture (ratio 50:50) unless otherwise stated.

Most technical grades of cypermethrin contain more than 90% of the active material. The material varies in physical form from a brown-yellow viscous liquid to a semi-solid.

Cypermethrin has a very low vapour pressure and solubility in water, but it is highly soluble in a wide range of organic solvents. Analytical methods are available for the determination of cypermethrin in commercially available preparations. In addition, methods for the determination of residues of cypermethrin in foods and in the environment are well established. In most substrates, the practical limit of determination is 0.01 mg/kg.

Environmental transport, distribution and transformation

Unlike the natural pyrethrins, cypermethrin is relatively stable to sunlight and, though it is probable that photodegradation plays a significant role in the degradation of the product on leaf surfaces and in surface waters, its effects in soils are limited. The most important photodegradation products, 2,2-dimethyl-3-(2,2-dichlorovinyl) cyclopropane-carboxylic acid (CPA), 3-phenoxybenzoic acid (PBA) and, to some extent, the amide of the intact ester, do not differ greatly from those resulting from biological degradation.

Degradation in the soil occurs primarily through cleavage of the ester linkage to give CPA, PBA, and carbon dioxide. Some of the carbon dioxide is formed through the cleavage of both the cyclopropyl and phenyl rings under oxidative conditions. The half-life of cypermethrin in a typical fertile soil is between 2 and 4 weeks.

Cypermethrin is adsorbed very strongly on soil particles, especially in soils containing large amounts of clay or organic matter. Movement in the soil is therefore extremely limited and downward leaching of the parent molecule through the soil does not occur to an appreciable extent under normal conditions of use. The two principal degradation products show, on the scale of Helling, 'intermediate mobility'.

Cypermethrin is also relatively immobile in surface waters and, when applied to the surface of a body of water at rates typical of those used in agriculture applications, it is largely confined to the surface film and does not reach deeper levels or the sediment in appreciable concentrations. Cypermethrin also degrades readily in natural waters with a typical half-life of about 2 weeks. It is probable that both photochemical and biological processes play a part. It has been shown that spray drift reaching surface waters adjacent to sprayed fields does not result in long-term residues in such waters.

Accumulation studies have shown that cypermethrin is rapidly taken up by fish (accumulation factor approximately 1000); the half-life of residues in rainbow trout was 8 days. In view of the low concentrations of cypermethrin that are likely to arise in water bodies and their rapid decline, it has been concluded that, under practical conditions, residues in fish will not reach measurable levels.

The results of field studies have shown that, when applied at recommended rates, the levels of cypermethrin and its degradation products in soil and surface waters are very low. Thus, it is unlikely that the recommended use of cypermethrin will have any effects on the environment.

Environmental levels and human exposure

Cypermethrin is used in a wide range of crops. In general, the maximum residue limits are low, ranging from 0.05 to 2.0 mg/kg in the different food commodities. The residues will be further reduced during food processing. In food of animal origin, residues may range between 0.01 and 0.2 mg/kg product. Residues in non-food commodities are generally higher, ranging up to 20 mg/kg product.

Total dietary intake values for man are not available, but it can be expected that the oral exposure of the general population is low to negligible.

Kinetics and metabolism

Absorption of cypermethrin from the gastrointestinal tract and its elimination are quite rapid. The major metabolic reaction is cleavage of the ester bond. Elimination of the cyclopropane moiety in the rat, over a 7-day period, ranged from 40 to 60% in the urine and from 30 to 50 % in the faeces; elimination of the phenoxybenzyl moiety was about 30% in the urine and 55 to 60 % in the faeces. Biliary excretion is a minor route of elimination for the cyclopropane moiety and small amounts are exhaled as carbon dioxide. In principle, these absorption and elimination rates and metabolic pathways hold for all animal species studied, including domestic animals. In cows fed 100 mg cypermethrin/day, the highest level found in milk was 0.03 mg/litre; levels of up to 0.1 mg/kg tissue were found in subcutaneous fat. Under practical conditions, the oral intake of cypermethrin with feed will be much lower. Cypermethrin used as a spray or dip to combat parasites, may give rise to maximum residues of 0.05 mg/kg tissue and 0.01 mg/litre milk.

Laying hens exposed orally to 10 mg cypermethrin/kg diet for 2 weeks, showed cypermethrin levels of up to 0.1 mg/kg in the fat, and up to 0.09 mg/kg in the eggs (predominantly in the yolk).

Consistent with the lipophilic nature of cypermethrin, the highest mean tissue concentrations are found in body fat, skin, liver, kidneys, adrenals, and ovaries. Only negligible concentrations are found in the brain. The half-life of *cis*-cypermethrin in the fat of the rat ranges from 12 to 19 days and that of the *trans*-isomer, from 3 to 4 days. In mice, these half-lives are 13 days and 1 day, respectively.

Overall, the metabolic transformation has been similar in the different animals studied, including man. Differences that occur have been related to the rate of formation rather than to the nature of the metabolites formed and to conjugation reactions. Cypermethrin (both the *cis*- and *trans*-isomers) is metabolized via the cleavage of the ester bond to phenoxybenzoic acid and cyclopropane carbolic acid. The fact that thiocyanate has been identified in *in vivo* studies, indicates that the cyanide moiety is further metabolized. The 3-phenoxybenzoic acid is mainly excreted as a conjugate. The type of conjugate differs in a number of animal species. Phenoxybenzoic acid is further metabolized to a hydroxy derivative and conjugated with glucuronic acid or sulphate. The cyclopropyl moiety is mainly excreted as a glucuronide conjugate, hydroxylation of the methyl group only occurring to a limited extent.

Ester cleavage is much slower in certain fish species than in other animal species, the main metabolic pathway being hydroxylation of the phenoxybenzoic and the cyclopropyl moieties.

Ester cleavage also takes place in plants. The phenoxybenzyl and cyclopropyl moieties are readily converted into glucoside conjugates. In mammals, these conjugates are hydrolysed into the original acids and metabolized.

Effects on organisms in the environment

High doses of cypermethrin may exert transient minor effects on microflora activity in the soil. However, no influence on ammonification and nitrification has been found.

Cypermethrin is very toxic for fish (in laboratory tests 96-h LC_{50}s were generally within the range of 0.4-2.8 μg/litre), and aquatic invertebrates (LC_{50}s in the range of 0.01-> 5 μg/litre). The presence of suspended solids decreases the toxicity by at least a factor of 2, because of adsorption of cypermethrin to the solids.

Cypermethrin is not very toxic for birds. Signs of cypermethrin intoxication were seen at dose levels of 3000 mg/kg body weight or more. Administration of 1000 mg cypermethrin/kg body weight to laying hens over a 5-day period did not cause signs of intoxication. However, cypermethrin was highly toxic for honey bees in laboratory tests, the oral LD_{50} ranging from 0.03 to 0.12 μg/bee. Under field conditions, the hazard is considerably lower, because of the repellent effect of cypermethrin on worker honey bees, which lasts for at least 6 h after spraying.

Earthworms are not sensitive to cypermethrin. No deaths occurred in worms exposed to levels of 100 mg/kg soil for 14 days.

In studies involving deliberate overspraying of experimental ponds under field conditions, peak concentrations of 2.6 μg cypermethrin/litre were measured in the water. Fish were not affected, but populations of crustaceae, mites, and surface-breathing insects were severely reduced. Most of these populations returned to normal levels after 15 weeks. Free-swimming, dipterous larvae and bottom-dwelling invertebrates, snails, flatworms, etc., were not affected. Under normal agricultural conditions (during which drifts may reach adjacent ditches or streams), the only effects seen in surface-breathing or surface-dwelling insects were hyperactivity or immobilization.

The relative toxicity of cypermethrin for pests and their parasites and predators is such that the balance between host/prey and parasites/predator may not be adversely affected in the field. However, care should be taken where predatory mites are important in pest management.

Effects on experimental animals and in vitro *test systems*

The acute oral toxicity of cypermethrin is moderate. While LD_{50} values differed considerably among animal species depending on the vehicle used and the *cis-/trans*-isomeric ratios, the toxic responses in all species were found to be very similar. The acute toxicity of the *trans*-isomer in the rat (LD_{50} > 2000 mg/kg body weight) was lower than that of the *cis*-isomer (LD_{50} 160-300 mg/kg body weight). The onset of toxic signs of poisoning was rapid and they disappeared within several days in survivors. The toxic signs are characterized by salivation, tremors, increased startle response, sinuous writhing of the whole body (choreoathetosis), and clonic seizures. Myelin and axon degeneration were noted in the sciatic nerve at near lethal dose levels.

Cypermethrin was moderately to severely irritating, when applied to the skin or the eye of the rabbit. The severity was partly dependent on the vehicle used. In guinea-pigs, a mild skin sensitizing potential was found using the maximization test.

No toxic effects were observed in rats, fed cypermethrin at 100 mg/kg diet for 3 months. Furthermore, prolonged feeding of cypermethrin (2 years) to dogs at a level of 300 mg/kg feed did not produce any toxicological effects. A level of 600 mg/kg diet resulted in reduced body weight gain, but no gross pathological or histopathological effects were seen.

Two long-term studies on rats and one on mice were carried out. The dose levels in the rat studies ranged up to 1500 mg/kg diet, equivalent to 75 mg/kg body weight. No effects were seen at 150 mg/kg diet. At the highest dose level, reduced body weight gain, increased liver weights (accompanied by increased smooth endoplasmatic reticulum), and some haematological and biochemical changes were observed. No increase in tumour incidence was noted. The same type of effects were seen in the mouse study at 1600 mg cypermethrin/kg diet. No effects were seen in the 400 mg/kg diet group.

The effects of cypermethrin on the immune system was studied in rats. The results showed the possibility of immune-suppression by pyrethroids. More attention should be paid to this aspect, but, at present, no opinion can be given about its relevance in the extrapolation of these data for man.

Repeated oral administration of cypermethrin to rats and other animal species at levels sufficiently high to produce significant mortality in one group of animals, produced biochemical changes in the peripheral nerves, consistent with sparse axonal degeneration. Histopathological changes (swelling and/or disintegration of axons of the sciatic nerve) were observed. There was no cumulative effect. The magnitude of the change was substantially less than that encountered with established neurotoxic agents. The neurotoxic effects seem to be reversible; presumably the clinical signs are not related to the induction of neuro-pathological lesions.

Further evidence to support the minor nature of the nerve lesions has been afforded by electrophysiological studies on rats. Measurements of the maximal motor conduction velocities of the sciatic and tail nerves of rats were made before, and at intervals of up to 5 weeks after, exposure to a single dose or repeated high doses of cypermethrin. It was concluded from the results that, even at near-lethal doses, cypermethrin did not cause any effects on maximal motor conduction velocities and conduction velocities of the slower motor fibres in rat peripheral nerves. No delayed neurotoxicity was observed in domestic hens.

The ability of the major metabolite of cypermethrin, 3-phenoxybenzoic acid, to produce axonal changes has been investigated and found to be negative.

In a multigeneration reproduction study on rats, dose levels up to 500 mg/kg feed were tested. The parent animals at the highest dose level showed decreased food intake and reduction in body weight gain. No influence on reproductive performance or on survival of the offspring was found. However, at the highest dose level, reductions in litter size and total litter weights were seen. The pooled body weights of weaning pups of the 500 mg/kg group were decreased over 3 generations. No effect was found with 100 mg cypermethrin/kg diet.

Embryotoxic and teratogenic effects were not found in rats administrated dose levels of up to 70 mg/kg body weight and clear teratogenic effects were not observed in rabbits given dose levels of up to 30 mg/kg body weight during days 6-18 of gestation.

Cypermethrin did not show any mutagenic activity in bacteria or in yeast, with or without metabolic activation,

or in V_{79} Chinese hamster cells. Furthermore, cypermethrin gave negative results in an *in vivo* chromosomal aberration test with Chinese hamsters and in dominant lethal studies on mice. In a host-mediated assay with mice, no increase in the rate of mitotic gene conversion in *Saccharomyces cerevisae* was found. In a chromosome study using the bone marrow cells of Chinese hamsters, cypermethrin did not increase the number of chromosome abnormalities. However, in a micronucleus test with mouse bone marrow cells, an increase in the frequency of polychromatic erythrocytes with micronuclei was found after oral and dermal applications of cypermethrin. Intraperitoneal application gave a negative result. A sister chromatid exchange study using bone marrow cells of mice showed a dose-response related increase in sister chromatid exchanges of dividing cells.

In long-term carcinogenicity studies, oral administration of cypermethrin to rats did not induce an increase in the incidence of tumours. In a mouse study, dose levels of up to 1600 mg cypermethrin/kg diet did not produce any increase in tumours of types not commonly associated with the mouse strain employed. The incidence of tumours was similar in all groups with the exception of a slight increase in the incidence of benign alveolar lung tumours in the females in the 1600 mg/kg diet group. However, the increased incidence, when compared with concurrent and historical control incidence, was not sufficient to warrant concern. There was no suggestion of increased malignancy and no evidence of a decrease in the latency of the tumours. Furthermore, there was no evidence of a carcinogenic response in the male mice in this study and, as the results of mutagenicity studies on cypermethrin have been mainly negative, it is concluded that there is no evidence for the carcinogenic potential of cypermethrin.

Mechanism of toxicity

Extensive studies have been carried out to explain the mechanism of toxicity of cypermethrin, especially with regard to the effects on the nervous system. The results strongly suggest that the primary target site of cypermethrin (and of pyrethroid insecticides in general) in the vertebrate nervous system is the sodium channel in the nerve membrane. The α-cyano pyrethroids, such as cypermethrin, cause a long-lasting prolongation of the normally transient increase in sodium permeability of the nerve membrane during excitation, resulting in long-lasting trains of repetitive impulses in sense organs and a frequency-dependent depression of the nerve impulse in nerve fibres. Since the mechanisms responsible for nerve impulse generation and conduction are basically the same throughout the entire nervous system, pyrethroids may well act in a similar way in various parts of the central nervous system. It is suggested that the facial skin sensations that may be experienced by people handling cypermethrin are brought about by repetitive firing of sensory nerve terminals in the skin, and may be considered as an early warning signal that exposure has occurred.

Effects on man

No cases of accidental poisoning have been reported as a result of occupation exposure.

Skin sensations, reported by a number of authors to have occurred during field studies, generally lasted only a few hours and did not persist for more than one day after exposure. Neurological signs were not observed. General medical and extensive clinical blood-chemistry studies, and electrophysiological studies on selected motor and sensory nerves in the legs and arms did not show any abnormalities.

Conclusions

General population exposure: Under recommended conditions of use the exposure of the general population to cypermethrin is negligible and is unlikely to present a hazard.

Occupational exposure: With reasonable work practices, hygiene measures, and safety precautions, the use of cypermethrin is unlikely to present a hazard to those occupationally exposed to it. The occurrence of 'facial sensations' is an indication of exposure. Under these circumstances work practices should be reviewed.

Environment: With recommended application rates, it is unlikely that cypermethrin or its degradation products will attain levels of environmental significance. The fact that cypermethrin is highly toxic for fish and honey bees is only likely to cause a problem in the case of spillage or overspraying.

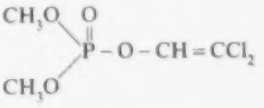
Sources: 1. 'Environmental Health Criteria 82: Cypermethrin.' International Programme on Chemical Safety, World Health Organization, CH-1211 Geneva 27, Switzerland (1989)

2. 'Health and Safety Guide No. 22 Cypermethrin.' International Programme on Chemical Safety (1989).

Dichlorvos

The International Programme on Chemical Safety has published an Environmental Health Criteria document on dichlorvos. An International Task Group discussed and finalized the document at a meeting held in Geneva. In addition a Health and Safety Guide (HSG) on dichlorvos has recently been made available. A summary of the findings of the Tast Group and the Conclusions of the HSG are given below.

Identity

Common name:		Dichlorvos
Chemical names:	CAS	2,2-dichloroethenyl dimethylphosphate
	IUPAC	2,2-dichlorovinyl dimethylphosphate
Synonyms and trade names:		Bayer-19149; C-177: DDVF; DDVP; Dedevap; ENT-20738; Nogos; Nuvan; OMS-14; Phosvit; SD 1750; Vaponal
Chemical structure:		
Molecular formula:		$C_4H_7Cl_2O_4P$
Registry numbers:	CAS	62-73-7
	RTECS	TC 0350000

Properties and use

Dichlorvos, an organophosphate, is a direct-acting cholinesterase[1] (ChE) inhibitor. Since 1961, it has been commercially manufactured and used throughout the world as a contact and stomach insecticide. It is used to protect stored products and crops (mainly in greenhouses), and to control internal and external parasites in livestock (granules of impregnated resin) and insects in houses, buildings, aircraft, and outdoor areas (as aerosols, liquid sprays, or impregnated cellulosic, ceramic, or resin strips). The present worldwide production of dichlorvos is about 4 million kg per year.

The purity of the technical grade product is at least 97%, and the type of impurities depends on the manufacturing process. In the presence of moisture, dichlorvos breaks down to form acidic products that are eventually mineralized. Technical dichlorvos may be stabilized, which improves the storage stability, but it is not normally necessary to stabilize high purity products. In the past, 2 – 4% epichlorohydrin has been used for this purpose. Dichlorvos is soluble in water and miscible with most organic solvents and aerosol propellants. The vapour pressure of dichlorvos is relatively high (1.6 Pa at 20 °C).

Methods for sampling and analysing dichlorvos in food, feed, and the environment and for determining the inhibition of ChE activity in blood, red blood cells, plasma, and brain are described.

Environmental transport, distribution, and transformation

Dichlorvos is not directly applied to soil, but is added to water to control invertebrate fish parasites encountered during intensive fish farming. It breaks down rapidly in humid air, water, and soil, both by abiotic and biotic processes, whereas on wooden surfaces it may persist for a longer time (39% remaining after 33 days). It degrades mainly to dichloroethanol, dichloroacetaldehyde (DCA), dichloroacetic acid, dimethylphosphate, dimethylphosphoric acid, and other water-soluble compounds, which are eventually mineralized.

Dichlorvos is rapidly lost from leaf surfaces by volatilization and hydrolysis.

Accidental spillage of dichlorvos may have acute hazardous effects on man and the environment. However, long-term effects are unlikely, in view of the volatility and initability in humid environments. Bioaccumulation or biomagnification do not occur.

Environmental levels and human exposure

The indoor air dichlorvos concentrations resulting from household and public health use depend on the method of application, temperature, and humidity. For example, one impregnated resin strip per 30 m^3 results in concentrations of the order of 0.1-0.3 mg/m^3 the first week (the latter only in special circumstances), subsequently decreasing to 0.02 mg/m^3 or less over the next few weeks.

Dichlorvos residues in food commodities are generally low and are readily destroyed during processing. The metabolite DCA may also be present in detectable amounts. Total-diet studies in the UK and the USA have confirmed that no, or very little, dichlorvos is found in prepared meals.

Exposure of the general population via food and drinking-water as a result of agricultural or post-harvest use of dichlorvos is negligible. However, household and public health use do give rise to exposure, principally through inhalation and dermal absorption.

Similar routes of exposure occur in professional pest control with dichlorvos. In warehouses, mushroom houses, and greenhouses, the concentrations of dichlorvos in the air are in general below 1 mg/m^3 when the recommended application rates are used, but in certain circumstances they may rise considerably above this level.

Kinetics and metabolism

Dichlorvos is readily absorbed via all routes of exposure. After oral administration, it is metabolized in the liver before it reaches the systemic circulation.

One hour after the oral administration of ^{32}P-dichlorvos, maximum concentrations of radioactivity are found in the kidneys, liver, stomach, and intestines. In bone, the increase is slower, due to inorganic phosphate entering the phosphate pool of the organism.

Pigs administered a single oral dose of ^{14}C-labelled dichlorvos as a slow-release polyvinyl chloride (PVC) formulation, showed radioactivity in all tissues, the highest level being in the liver after 2 days, and the lowest being in the brain. Pregnant sows were fed vinyl-1-^{14}C-dichlorvos or ^{36}Cl-dichlorvos in PVC pellets at 4 mg dichlorvos/kg body weight per day during the last third of the gestation period. Although the tissues of the sows and piglets contained ^{14}C or ^{36}Cl ranging from 0.3 to 18 mg/kg tissue, no radioactivity was associated with dichlorvos or its primary metabolites.

Up to 70% of the dichlorvos inhaled by pigs is taken up into the body. When rats and mice inhaled dichlorvos (90 mg/m^3 for 4 h), none or very little (up to 0.2 mg/kg) was found in blood, liver, testes, lung, or brain. The highest concentrations (up to 2.4 mg/kg tissue) were found in kidneys and adipose tissue. Dichlorvos rapidly disappeared from the kidneys with a half-life of approximately 14 min.

Dichlorvos is metabolized mainly in the liver via two enzymatic pathways: one, producing desmethyldichlorvos, is glutathione dependent, while the other, resulting in dimethyl-phosphate and DCA, is glutathione independent. The metabolism of dichlorvos in various species, including man, is rapid and uses similar pathways. Differences between species relate to the rate of metabolism rather than to a difference of metabolites.

The major route of metabolism of the vinyl portion of dichlorvos leads to (a) dichloroethanol glucuronide and (b) hippuric acid, urea, carbon dioxide, and other endogenous chemicals, such as glycine and serine, which give rise to high levels of radioactivity in the tissues. No evidence of the accumulation of dichlorvos or potentially toxic metabolites has been found.

The major route for the elimination of the phosphorus-containing moiety is via the urine, with expired air being a less important route. However, the vinyl moiety is mainly eliminated in the expired air, and less so in the urine. In cows, elimination is roughly equally distributed between urine and faeces.

Effects on organisms in the environment

The effect of dichlorvos on microorganisms is variable and species dependent. Certain microorganisms have the

[1] Cholinesterase is the enzyme which breaks down acetylcholine (ACh), the transmitter at cholinergic nerve synapses.

ability to metabolize dichlorvos but the pesticide may interfere with the endogenous oxidative metabolism of the organism. In certain organisms it causes growth inhibition, while in others it has no influence or may even stimulate growth. Dichlorvos has little or no toxic effect on microorganisms degrading organic matter in sewage. The above effects have been seen over the wide dose range of 0.1-100 mg/litre.

The acute toxicity of dichlorvos for both freshwater and estuarine species of fish is moderate to high (96-h LC_{50} values range from 0.2 to approximately 10 mg/l). Brain and liver ChE inhibition in certain fish was found at dose levels of 0.25-1.25 mg/l, but recovery of ChE activity took place when they were returned to clean water.

Invertebrates are more sensitive to dichlorvos. Levels above 0.05 μg/l may have deleterious effects. Dichlorvos also has a high oral toxicity for birds. The LD_{50} values are in the range of 5-40 mg/kg body weight. In short-term dietary studies, the compound was slightly to moderately toxic for birds. Brain ChE inhibition was seen at 50 mg/kg diet or more and at 500 mg/kg diet, half of the birds died. There have been instances when chickens and ducks have died after accidental access to dichlorvos-contaminated feed and drinking-water.

Dichlorvos is highly toxic for honey bees. The LD_{50} by oral administration is 0.29 μg/g bee, and after topical application is 0.65 μg/g bee.

Effects on experimental animals and in vitro *test systems*

Dichlorvos is moderately to highly toxic when administered in single doses to a variety of animal species by several routes. It directly inhibits acetylcholinesterase (AChE) activity in the nervous system and in other tissues. Maximum inhibition generally occurs within 1 h, and is followed by rapid recovery. The oral LD_{50} for the rat is 30-110 mg/kg body weight, depending on the solvent used. The hazard classification of dichlorvos by WHO is based on an oral LD_{50} for the rat of 56 mg/kg body weight. The signs of intoxication are typical of organophosphorus poisoning, i.e., salivation, lachrymation, diarrhoea, tremors, and terminal convulsions, with death occurring from respiratory failure. The signs of intoxication are usually apparent shortly after dosing, and, at lethal doses, death occurs within 1 h. Survivors recover completely within 24 h. Potentiation is slight when dichlorvos is given orally in combination with other organophosphates, but in combination with malathion it is marked.

In short-term toxicity studies on the mouse, rat, dog, pig, and monkey, inhibition of plasma, red blood cell, and brain ChE are the most important signs of toxicity. After oral administration, approximately 0.5 mg/kg body weight (range, 0.3-0.7 mg/kg) did not produce ChE inhibition. In a 2-year study on dogs, ChE inhibition was noted at 3.2 mg/kg body weight or more.

Flea collar dermatitis has been described in dogs and cats wearing dichlorvos-impregnated PVC flea collars. This was a primary irritant contact dermatitis which may have been caused by dichlorvos.

Many short-term inhalation studies on different animal species have been carried out. Air concentrations in the range of 0.2-1 mg/m³ do not affect ChE activity significantly. Other effects, such as growth inhibition and increase in liver weight have been reported at dose levels at least 10-20 times higher.

It is possible to produce clinical neuropathy in hens, but the doses of dichlorvos required are far in excess of the LD_{50}. The effects are associated with high inhibition of neurotoxic esterase (NTE) in the brain and spinal cord. In the rat, however, neuropathic changes in the white matter of the brain have been reported following repeated daily oral application of an LD_{50} dose.

Immune suppression has been reported in rabbits. At present, no evaluation as to the relevance for human beings can be given; more attention to this aspect is needed.

In a long-term study, rats fed dichlorvos in the diet for 2 years showed no signs of intoxication. Hepatocellular fatty vacuolization of the liver and ChE inhibition were significant at the two highest dose levels (2.5 and 12.5 mg/kg body weight).

In a carefully conducted long-term inhalation study on rats with whole body exposure (23 h/day, for 2 years), results were comparable with those seen in the oral study. No effects were seen at 0.05 mg/m³, inhibition of ChE activity took place at 0.48 mg/m³ or more.

In several reproduction studies on rats and domestic animals, no effects were seen on reproduction, and there was no embryotoxicity at dose levels that did not cause maternal toxicity. At toxic doses, dichlorvos may cause reversible disturbances of spermatogenesis in mice and rats. It was not teratogenic in several studies carried out on rats and rabbits.

Dichlorvos is an alkylating agent and binds *in vitro* to bacterial and mammalian nucleic acids. It is mutagenic in a number of microbial systems, but there is no evidence of mutagenicity in intact mammals, where it is rapidly degraded by esterases in blood and other tissues.

Dichlorvos carcinogenicity has been investigated in mice (oral studies) and rats (oral and inhalation studies). The dose levels used in 2-year oral studies were up to 800 mg/l drinking-water or 600 mg/kg diet for mice, and up to 280 mg/l drinking-water or 234 mg/kg diet for rats. In a rat inhalation study, dichlorvos concentrations in air of up to 4.7 mg/m³ were tested for 2 years. No statistically significant increase in tumour incidence was found. In two recent carcinogenicity studies on mice and rats, dichlorvos was administered by intubation at dose levels between 10 and 40 mg/kg body weight (mice) and 4 and 8 mg/kg body weight (rat) for up to 2 years. Only preliminary information has been provided. The evidence for carcinogenicity in these new studies is difficult to interpret at this time. Only when complete and final reports become available will it be possible to draw more definitive conclusions.

From acute and short-term studies, it is clear that the metabolites of dichlorvos are all less toxic than the parent compound. Only DCA was positive in a few mutagenicity tests.

Effects on man

A fatal case of dichlorvos poisoning has been described in the general population: despite correct treatment, a suicide succeeded with approximately 400 mg dichlorvos/kg body weight. In another poisoning case, a woman ingested about 100 mg dichlorvos/kg and survived, following intensive care for 14 days. Two workers who had skin exposure to a concentrated dichlorvos formulation, and failed to wash it off, died of poisoning.

There have been two clinical reports describing four patients suffering from severe poisoning from dichlorvos, taken orally, who survived after treatment and who showed

delayed neurotoxic effects. Thus, although the possibility of neuropathy in man cannot be excluded, it is likely to occur only after almost lethal oral doses.

Since the 1960s, field studies in malaria control have been carried out and the interiors of aircraft have been sprayed with dichlorvos. Exposure to air concentrations of up to 0.05 mg/m³ were without clinical effects, and no, or only insignificant, inhibition of blood ChE activity was noted.

When dichlorvos was administered orally to human volunteers (single or repeated doses of a slow-release PVC formulation), significant inhibition of red blood cell ChE activity was found at 4 mg/kg body weight or more. At 1 mg/kg body weight or more, plasma ChE activity was significantly inhibited. Daily oral doses of 2 mg dichlorvos/person for 28 days reduced plasma ChE activity by 30%, but red cell ChE activity was unaffected.

Human volunteers who were exposed to dichlorvos by inhalation for a certain period per day for a number of consecutive days or weeks showed ChE inhibition at a concentration of 1 mg/m³ or more, but not at 0.5 mg/m³. These results were confirmed in studies with pesticide operators who came into contact with dichlorvos.

Hospitalized patients showed similar results after oral administration or exposure by inhalation. Sick adults and children and healthy pregnant women and babies in hospital wards treated with dichlorvos strips (1 strip per 30 or 40 m³) displayed normal ChE activity. Only subjects exposed 24 h/day to concentrations above 0.1 mg/m³ or patients with liver insufficiency showed a moderate decrease in plasma ChE activity.

No significant effects on plasma or red blood cell ChE activity were observed in people exposed to the recommended rate of one dichlorvos strip per 30 m³ in their homes over a period of 6 months, even when the strips were replaced at shorter intervals than that normally recommended. The maximum average concentration in the air was approximately 0.1 mg/m³.

In factory workers exposed to an average of 0.7 mg/m³ for 8 months, significant inhibition of plasma and red blood cell ChE activity was found.

Cases of dermatitis and skin sensitization due to dichlorvos have been described in workers handling and spraying different types of pesticides. In addition cross-sensitization with certain pesticides has been seen.

Conclusions

(a) Exposure of the general population to dichlorvos through food and drinking-water is negligible and does not constitute a health hazard.

(b) The in-house use of dichlorvos as an insecticide in the form of sprays or slow-release strips, at recommended levels of use, does not constitute a short- or a long-term hazard for the general population. However, continous (24 h per day) exposure of young children and sick or elderly people in non- or poorly-ventilated rooms should be avoided.

(c) Notwithstanding their toxicity, dichlorvos and its formulations do not present an undue hazard for those occupationally exposed, when adequate ventilation and skin protection are used.

(d) Except in the case of gross spillage, the recommended use of dichlorvos as an insecticide dose not pose any acute or long-term hazards for aquatic and terrestrial organisms, though there may be an acute hazard for birds and bees.

Recommendations

(a) Continous (24 h/day) exposure of young children and sick or elderly people to dichlorvos in non- or poorly-ventilated rooms should be avoided.

(b) As dichlorvos from various sources may differ in purity and impurities, attention should be paid to its composition. This should conform to FAO and WHO specifications. In the case of formulations, other components, such as solvents and stabilizers, should also be considered.

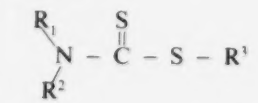
Sources: 1. 'Environmental Health Criteria No. 79: Dichlorvos.' International Programme on Chemical Safety, World Health Organization, CH-1211 Geneva 27, Switzerland (1989).

2. 'Health and Safety Guide No. 18, Dichlorvos.' International Programme on Chemical Safety, World Health Organization, CH-1211 Geneva 27, Switzerland (1988).

Dithiocarbamates

The International Programme on Chemical Safety (IPCS) has published an Environmental Health Criteria document on dithiocarbamate pesticides, ethylenethiourea, and propylenethiourea. An International Task Group discussed and finalized the document at a meeting held in Hanover, Federal Republic of Germany. A summary of the findings of the Task Group on dithiocarbamates is given below. Summaries of ethylenethiourea and propylenethiourea are given on page 32 of this Bulletin.

Dithiocarbamates are disulphur analogues of carbamates. The general formula of dithiocarbamates is characterized by the presence of:



Properties, uses and analytical methods

Dithiocarbamates with hydrophylic groups form water-soluble, heavy-metal complexes, while some of the dithiocarbamate metal complexes used as fungicides are insoluble in water but soluble in non-polar solvents. Alkylene bisdithiocarbamates (containing two donor CS_2 groups), which form polymeric chelates, are insoluble in both water and non-polar solvents.

The heavy-metal salts of ethylene bisdithiocarbamic acid may polymerize. Dithiocarbamates may decompose under certain circumstances into a number of compounds, such as sulphur, 5,6-dihydro-*3H*-imidazol [2,1-C]-1, 2,4-dithiazole-3-thione, ethylenethiourea (ETU), and ethylenediamine (EDA). ETU is fairly stable, has a high water solubility, and is of particular importance because of its specific toxicity.

Dithiocarbamates are mainly used in agriculture as insecticides, herbicides, and fungicides. Additional uses are as biocides for industrial or other commercial applications, and in household products. Some are used for vector control in public health.

Depending on the types of monoamines used in the synthesis of these compounds, mono- or dialkyldithiocarbamates are formed. Reactions with diamines result in the formation of two terminal dithiocarbamate groups linked by an alkylene (ethylene) bridge. Both alkyl and ethylene

dithiocarbamates form salts with metals, and both can be oxidized to the corresponding disulphides.

More than 15 dithiocarbamates are known. However, it is beyond the scope of this publication to give complete information on each compound. The intention is to cover the different aspects of dithiocarbamates, making use of publications and reports available on the compounds that are most used and best known. Data on the carbamates or thiocarbamates are not included, because these compounds have been covered in 'Environmental Health Criteria 64: Carbamate Pesticides' and '76: Thiocarbamate Pesticides'.

Sources, environmental transport and distribution

Most dithiocarbamates were developed during and after the Second World War. However, a few compounds (ziram and thiram) were introduced around 1931. Dithiocarbamates, with their insecticidal, herbicidal, and fungicidal properties, have a wide range of applications and are produced in great quantities. Because of their high biological activity, dithiocarbamates are also used in medicine, the rubber industry, and in the treatment of chronic alcoholism.

Alkyl dithiocarbamates are stable in an alkaline medium. By splitting off carbon disulphide and hydrogen sulphide, as well as by oxidative degradation, a number of break-down products, such as ETU, are formed in soil and water. The rate of degradation depends on a number of factors, including pH and type of cation. Ethylene bisdithiocarbamates (EBDCs) are generally unstable in the presence of moisture, oxygen, or biological systems, and decompose rapidly in water.

The mobility of EBDCs in soil varies considerably, depending on their individual water solubilities and the type of soil. ETU is water-soluble and mobile. It is taken up by plant roots, is translocated, and metabolized, forming ethyleneurea (EU), other 2-imidazole derivatives, and various unidentified metabolites. In addition, ETU is readily photo-oxidized to EU in the presence of photosensitizers. Residues of EBDCs and ETU are found in and/or on crops treated with EBDCs. The residue levels change during storage, processing, and cooking due to environmental factors. During these processes, the parent compound may be converted to ETU.

Environmental levels and human exposure

Information on the environmental impact of dithiocarbamates with respect to persistence and bioaccumulation in the different species and food chains is limited. On the basis of the available information, it is likely that most of these compounds are rapidly degraded in the presence of oxygen, moisture, etc., to form a number of compounds, some of which, e.g., ETU and propylenethiourea (PTU), are toxicologically important.

When certain crops, such as spinach, carrots, and potatoes, are treated with EBDCs, high levels of ETU can be found after cooking. In general, however, the ETU levels are below 0.1 mg/kg product.

Human exposure to EBDCs was calculated for the population of the USA on the basis of estimated consumption of dietary residues of ETU in treated crops. Upper limit (worst case) and lower limit (lowest case) estimates of exposure to ETU were 3.65 μg/kg and 0.24 μg/kg body weight per day, respectively. An estimate made for the Canadian population on the basis of results of available market-basket surveys would be around 1 μg/kg body weight per day.

Kinetics and metabolism

As a general rule, dithiocarbamates can be absorbed by the organism via the skin, mucous membranes, and the respiratory and gastrointestinal tracts. Whereas dithiocarbamates are absorbed rapidly from the gastrointestinal tract, metal-complexed alkylene bisdithiocarbamates are absorbed poorly both from the gastrointestinal tract and through the skin.

Dialkyldithiocarbamates and EBDCs are metabolized via different mechanisms. The metabolism of the former is straightforward, dialkylthiocarbamic acid being formed as a free acid or as *S*-glucuronide conjugate. Other metabolic products include carbon disulphide, formaldehyde, sulphate, and dialkylamine.

The metabolic decomposition of EBDCs in mammals is complex and results in the formation of carbon disulphide, EDA, a few ethylene bisthiuram disulphides, hydrogen sulphide, ethylene bisthiocyanate, and ETU. The latter is further broken down to moieties that are incorporated into compounds such as oxalic acid, glycine, urea, and lactose. Dithiocarbamates and their metabolic products are found in certain organs, such as the liver, the kidneys and, especially, the thyroid gland, but accumulation of these compounds does not take place because of their rapid metabolism.

After treating plants with dithiocarbamates, a large number of metabolites are found, including ETU, EU, imidazole derivatives, diisothiocyanates, diamines, disulphides, and other metabolites, that are still unknown.

Effects on organisms in the environment

Soil microorganisms are capable of metabolizing dithiocarbamates. From the limited information available, it seems that the breakdown products can affect enzyme activities, respiration, and nitrification at dose levels of the order of 10 mg/kg dry soil or more.

Dithiocarbamates have an LC_{50} of less than 1 mg/l for invertebrates (*Daphnia*) and between 1 and 4 mg/l for algae (*Chlorella*). The acute toxicity of dithiocarbamates for fish is rather high. In general, the acute LC_{50} of dialkyldithiocarbamates for fish is less than 1 mg/l, and that of EBDCs is in the range of 1-8 mg/l water. The sac fry and early fry stages of the rainbow trout have a higher sensitivity than other early life stages, and embryotoxic and teratogenic effects are induced by certain dithiocarbamates. However, bioaccumulation is low (bioconcentration factor < 100). The toxicity of ETU and EU for fish, *Daphnia*, *Chlorella*, and two bacterial species is very low, of the order of g/l.

Several dithiocarbamates were shown to intervene with testicular development and function and to cause nerve fibre degeneration in domestic fowl.

Information on the influence of dithiocarbamates on honey bees is lacking.

Effects on experimental animals and in vitro *test systems*

The acute oral and dermal toxicities of the different dithiocarbamates are generally low. Most compounds have a low volatility, and only limited information concerning inhalation toxicity is available. Local irritation of the respiratory tract occurs when dithiocarbamates are inhaled

as dust, which can also induce eye and dermal irritation. Some dithiocarbamates are sensitizing agents. ETU also has a low acute oral toxicity.

Many short- and long-term toxicity studies have been carried out on different dithiocarbamates. In rats, some dithiocarbamates tested at high dose levels induced dose-dependent adverse effects on the reproduction and endocrine structures and functions, thus reducing reproductive capacity. Some dithiocarbamates also showed effects on reproduction in birds.

In teratogenicity studies on mice and rats, dithiocarbamates induced an increase in resorption sites and somatic and skeletal malformations (cleft palate, hydrocephaly, and other abnormalities). The dose levels needed to produce these effects were usually higher than 200 mg/kg body weight in rats, and above 100 mg/kg body weight in mice.

In general, the results of mutagenicity studies with dithiocarbamates have been negative.

From the available long-term carcinogenicity studies on mice and rats, there is no clear indication of a carcinogenic effect. Some of the dithiocarbamates have shown a goitrogenic effect at high dose levels.

There is evidence that certain dithiocarbamates may be converted *in vivo* to *N*-nitroso derivatives, which are considered to be both mutagenic and carcinogenic. However, the levels of nitroso compounds that can be expected to result from the dietary intake of dithiocarbamate pesticide residues are negligible compared with those of the nitroso precursors, which occur naturally in food and drinking-water.

In rats, high levels of dithiocarbamates produce an increase in thyroid weight, a reduction in colloid in follicles, hyperplasia, and nodular goitre. These distinct morphological changes are in agreement with an increase in thyroid-stimulating hormone (TSH). Hypophyseal stimulation of the thyroid is the consequence of a decreased blood level of thyroxin, the synthesis of which is inhibited by dithiocarbamates. The thyroid hyperplasia induced by dithiocarbamates is largely reversible on cessation of exposure.

Another intriguing phenomenon is the induction of alcohol intolerance by most of the alkyldithiocarbamates. This phenomenom has been studies in rats and produced in man. It has even led to the use of disulfiram in the treatment of chronic alcoholism.

At dose levels above 50 mg/kg body weight, dithiocarbamates produce neurotoxic effects in rats and rabbits, characterized by ataxia and paralysis of the hind legs, and demyelination and degeneration of peripheral nerves. In birds, paralysis and muscular and peripheral nerve atrophy have also been observed.

Dithiocarbamates have been reported to cause a redistribution of heavy metals, e.g., lead and cadmium, in organs such as the brain. Furthermore, because of their chelating properties, these dithiocarbamates may have an effect on the function of enzymes containing metals, such as zinc and copper.

Effects on man

Regular contact with dithiocarbamates can cause functional changes in the nervous and hepatobiliary systems. Skin contact with dithiocarbamates may induce contact dermatitis, and some of these compounds will induce sensitization. Alcohol intolerance can be induced by certain dithiocarbamates.

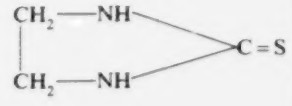
There are indications that the mean incidence of chromosomal aberrations in lymphocytes is increased in workers exposed to certain dithiocarbamates. Epidemiological studies on workers exposed to dithiocarbamates or ETU did not show any increase in the incidence of thyroid tumours. However, only a relatively small number of workers was involved.

Source: 'Environmental Health Criteria No. 78: Dithiocarbamate Pesticides ethylenethiourea, and propylenethiourea.' International Programme on Chemical Safety, World Health Organization, 1211 Geneva 27, Switzerland (1988).

Ethylenethiourea and propylenethiourea

The International Programme on Chemical Safety has published an Environmental Health Criteria document on dithiocarbamate pesticides, ethylenethiourea and propylenethiourea. An International Task Group discussed and finalized the document at a meeting held in Hanover, Federal Republic of Germany. A summary of the findings of the Task Group on ethylenethiourea and propylenethiourea is given below. Readers will find a summary of dithiocarbamate pesticides on page 30 of this Bulletin.

Ethylenethiourea

Identity	
Common name:	Ethylenethiourea
Synonyms and trade names:	Ethylene thiourea; N,N'-ethylenethiourea; ETU; 2-mercaptoimidazoune; 2-imidazolidinethione; NA-22-D; NCI-CO3372; Pennac CRA; 2-thiol-dihydroglyoxaline; urea, 1,3-ethylene-2-thio; USAF EL-62; Warecure C
Chemical structure:	
Molecular formula:	$C_3H_6N_2S$
Registry numbers: CAS	96-45-7
RTECS	NI 9625000

Ethylenethiourea is a white, crystalline solid and odourless substance. It has a melting point of 203-204 °C; it is soluble in water 20,000 mg/l at 30 °C, moderately soluble in ethanol, and nearly insoluble in chloroform.

Sources, environmental transport, and distribution

Ethylenethiourea (ETU) is found together with residues of the parent ethylene bisdithiocarbamates (EBDCs) in and on crops that have been treated with these pesticides. During storage, processing, and cooking, the amount of the parent compound decreases while that of ETU increases. ETU is easily photo-oxidized (in the presence of photosensitizers) to ethyleneurea (EU). One of the metabolic products of ethylene bisdithiocarbamate decomposition in mammals, plants and lower organisms is ETU.

Environmental levels and human exposure

In certain crops, such as spinach, carrots, and potatoes, treated with EBDCs, high levels of ETU can be found after cooking. In general, however, the ETU levels are below 0.1 mg/kg product.

Estimates of the exposure of the general population of the USA are of the order of 0.24-3.65 μg ETU/kg body weight per day and, in Canada, estimates based on market-basket studies are around 1 μg ETU/kg body weight per day.

Kinetics and metabolism

ETU is rapidly absorbed, metabolized, and excreted in mammals. Up to 90% is eliminated via the urine and only a small amount via the faeces. Distribution of ETU in the body appears to be fairly uniform with the exception of a relative accumulation in the thyroid. ETU is broken down to ethylene diamine (EDA), urea, carbon dioxide, or oxalic acid, or is transformed to imidazole derivatives in mammals, plants, and the environment.

Effects on organisms in the environment

The available LC_{50} levels of ETU and EU for fish are in the range of 7500-13,000 mg/l.

Effects on experimental animals and in vitro *test systems*

The acute oral toxicity in experimental animals is low, and the long-term effects are mainly characterized by an antithyroid action.

At dose levels >25 mg/kg body weight, decreases in serum T_3, T_4, and protein-bound iodine and increases in thyroid-stimulating hormone have been found in studies on experimental animals. At higher dose levels (>100 mg/kg body weight), increases in thyroid weight and hyperplasia occurred, which finally resulted in the development of adenocarcinoma. The effects of short-term exposure to low levels of ETU seem to be reversible, but those of long-term exposure to higher levels become, at a certain stage, irreversible. A level of approximately 5 mg/kg body weight seems to be without effects.

Most mutagenicity studies on ETU, especially those with mammalian test systems, have given negative results.

A number of carcinogenicity studies have been carried out on mice, rats, and hamsters. In addition to an antithyroid action, ETU has been found to induce, subsequently, thyroid tumours (hyperplastic goitre, solid-cell adenomas, and follicular and papillary carcinomas) in mice and rats. In an earlier study on mice, liver tumours, lung tumours, and lymphomas were also detected, but these findings have not been confirmed. No tumours except thyroid tumours have been found in rats, and in hamsters, no tumours of the thyroid gland or other organs were observed, even at 200 mg/kg diet.

At dose levels above approximately 10 mg/kg body weight, ETU has clear teratogenic effects in rats and hamsters, different types of central nervous system and skeletal anomalies being induced. However, in mice, no teratogenic effects were found at much higher dose levels (up to 800 mg/kg body weight).

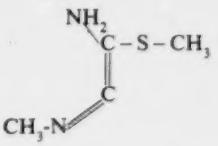
Effects on man

Epidemiological studies on workers exposed to ETU did not reveal any increase in the incidence of thyroid tumours.

Propylenethiourea

The metabolic products of propineb pesticide decomposition in mammals, plants, and lower organisms also give rise to propylenethiourea.

Identity

Common name:		Propylenethiourea
Synonyms and trade names:		4-methylethylenethiourea; 4-methyl-2-imidazolidinethione; propylene thiourea; PTU.
Chemical structure:		
Molecular formula:		$C_4H_8N_2S$
Registry numbers:	CAS	2122-19-2
	RTECS	NJ 0400000

In a long-term study on mice using propylenethiourea, an increased incidence of hepatocellular adenomas was observed at dose levels of 10 mg/kg diet or more. No thyroid tumours were found, but increased thyroid hypercellularity occurred at a dose level of 1000 mg/kg diet. In rats, goitrogenic effects were seen with PTU at dose levels as low as 1 mg/kg diet.

Source: 'Environmental Health Criteria No. 78: Dithiocarmate pesticides, ethylenethiourea, and propylenethiourea.' International Programme on Chemical Safety, World Health Organization, 1211 Geneva 27, Switzerland (1988)

Fluorides

The National Institute of Public Health and Environmental Protection of The Netherlands recently published a document on inorganic fluorides. Below we give a summary of this document.

It contains data on fluorides: their sources and distribution pattern (soil, water, air, biota); the risks based on a careful consideration of exposure levels and toxic concentrations; the technical possibilities of reducing these risks; and the economic consequences of any measures taken or proposed. This information provides the scientific basis for the formulation of the effect-directed standardization policy in The Netherlands.

Further study of the inorganic fluorides is called for because, for the time being, the extent and scale of their effects on public health, ecosystems, cultivated plants and livestock are not sufficiently well known. The extent to which fluoride accumulates and causes problems in the long term is also not sufficiently clear. However an attempt has been made to derive toxicological limit values to be used in the standard-setting policy.

In man, fluoride plays a role in the development of dentition and the skeleton. Although the data are insufficient for making a statement about the possible maximum acceptable atmospheric fluoride concentrations for man, it is concluded that the current concentrations indoors as well as outdoors (also around sources) will have no adverse effects on human health.

In fresh surface water a maximum concentration of 1.5 mg./l^{-1} (dissolved amount) has been proposed for aquatic organisms, on the basis of long-term toxicity studies. This level is also considered to be the maximum acceptable toxic concentration for humans and the occurrence of dental fluorosis, and has been proposed by the

EEC as an upper limit for surface waters intended for the production of drinking water.

In accordance with recent policy, the target value has been set at 1% of the maximum acceptable level (i.e., 0.01-0.015 mg./l^{-1}) or at the background level (0.01-0.3 mg./l^{-1}) when the target value to be derived is lower than the natural background concentration. The range of the lower limit therefore lies between 0.01 and 0.3 mg./l^{-1}.

In the marine environment, fluoride occurs naturally in high concentrations and accordingly belongs to the macrocomponents of seawater. Studies with a limited number of species of organisms support the assumption that intolerable effects are not to be expected when the concentration is less than 5 mg./l^{-1}.

Data on terrestrial ecosystems necessary for establishing a permissible concentration for soil or air are insufficient. For plants, the most critical route is exposure to atmospheric fluorides, while for animals the main intake source of fluoride is the diet. In view of the relatively high natural F concentrations in soil, the effect of F pollution on the soil flora and fauna does not appear to be the most critical consideration. The recommend values for the atmospheric fluoride concentrations are provisionally the same as those established for the protection of cultivated plants and domestic livestock. The uncertainty in these values is great and, because of the economic interests involved, require further study. Different levels of protection can be distinguished:

—0.05 μg F/m^{-3}, as a maximum annual average (pH 1 soluble fraction) during the whole year (thus also in winter) to protect flora and fauna;
—0.13 μg F/m^{-3}, as a maximum annual average (pH 1 soluble fraction) to protect (most) cultivated plants and wild flora;
—0.18 μg F/m^{-3} as a maximum annual average (seasonal average 0.13 μg.m^{-3} (pH 1 soluble fraction) to protect cattle and wild fauna during the grazing season.

There are no data indicating that fluorides are involved in pollutant damage to materials at current atmospheric concentrations, also worldwide effects on the biosphere are not to be expected.

Source: 'Integrated Criteria Document on Fluorides.' National Institute of Public Health and Environmental Protection, Antonie Van Leeuwenhoeklaan 9, P.O. Box 1, 3720 BA Bilthoven, The Netherlands (September 1989).

Pyrrolizidine alkaloids

The International Programme on Chemical Safety has published an Environmental Health Criteria document on pyrrolizidine alkaloids. An International Task Group discussed and finalized the document at a meeting held in Tashkent, USSR. In addition, a Health and Safety Guide (HSG) on pyrrolizidine alkaloids has recently been made available. A summary of the findings of the Task Group is given below.

The toxic pyrrolizidine alkaloids (PAs) are a large group of related compounds (about 160 are known) that occur in plants, mainly in species of *Crotalaria* (Leguminosae), *Senecio* and related genera (Compositae), *Heliotropium, Trichodesma, Symphytum, Echium,* and other genera of the Boraginaceae which occur throughout the world. The chemical structures of some alkaloids that are important in relation to disease are shown in the next column.

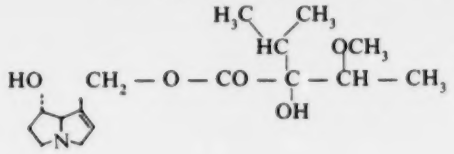
Properties and use

The pure alkaloids are mostly crystalline solids; some are gums or amorphous solids. Some are only slightly soluble in water, but all dissolve when neutralized with acid. They occur in the plants partly as *N*-oxides, which are water soluble. The alkaloids are fairly stable, but are subject to hydrolysis in alkaline solution and to enzymatic decomposition. The latter occurs in some plant species during wilting and drying. The stability of the alkaloids when the plants are cooked is not known.

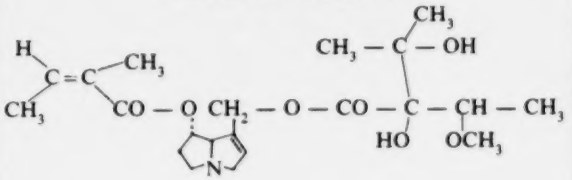
The ingestion of PAs in foods and medicinal herbs results in acute and chronic effects in man, affecting mainly the liver. Data from experimental animal studies indicate that PAs represent a potential cause of cancer in man.

Identity

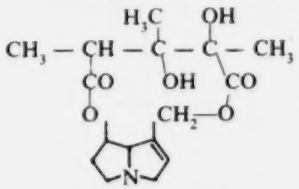
Heliotropine $C_{16}H_{27}NO_5$
CAS Registry No. 303-33-3



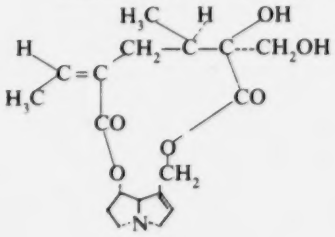
Lasiocarpine $C_{21}H_{33}NO_7$
CAS Registry No. 303-34-4



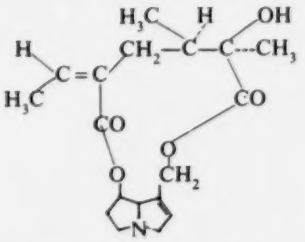
Monocrotaline $C_{16}H_{23}NO_6$
CAS Registry No. 315-22-0



Retrorsine $C_{18}H_{25}NO_3$
CAS Registry No. 480-54-6



Senecionine $C_{18}H_{25}NO_5$
CAS Registry No. 130-01-8



The hepatotoxic alkaloids have a 1,2-double bond in the pyrrolizidine ring and branched chain acids, esterifying a 9-hydroxyl and preferably also the 7-hydroxyl substituent. Modified seco-pyrrolizidine alkaloids, in which the central bond between the N and C8 atoms is broken, are also hepatotoxic. Some *Senecio* species contain non-basic derivatives that are 5-oxopyrroles. The toxicity of these derivatives may be similar to that of the alkaloids, but this aspect has not been investigated. The alkaloids occur as free bases and *N*-oxides. The latter are reduced to the free bases in the gastrointestinal tract of animals and have a similar toxicity when ingested orally.

Suitable analytical procedures are available for screening plant species, including a simple field test for toxic alkaloids. Thin-layer chromatography (TLC), high-performance liquid chromatography (HPLC), gas chromatography (GC), and gas chromatography-mass spectrometry (GC-MS) have been applied for separating, characterizing, and quantifying the alkaloids present. Effective use of these procedures requires authentic alkaloids for standards, few of which are available. Improved analytical methods are required for the determination of very low levels of alkaloids in some foodstuffs.

Mechanisms and features of toxicity

The toxic effects of PAs are due to activation in the liver. Metabolism of the alkaloids by mixed-function oxidases leads to pyrrolic dehydro-alkaloids, which are reactive alkylating agents. Reaction of initial metabolites with constituents of the liver cell in which they are formed are probably the main cause of liver cell necrosis. Metabolites are released into the circulation and are believed to pass beyond the liver to the lung causing vascular lesions characteristic of primary pulmonary hypertension, especially when alkaloids, such as monocrotaline, are administered to animals.

In experimental animals, PAs are quickly metabolized and are almost completely excreted in 24 h, so that no residual products are detectable in the biological fluids or body tissues after this period. The rate of formation of pyrrolic metabolites is influenced by the induction or inhibition of the mixed-function oxidases in the liver, but the relationship between the rate of metabolism and expression of toxicity is uncertain.

Several pyrrolizidine alkaloid-derivatives and related compounds are known to cause chromosome aberrations in plants, leukocyte cell cultures of the marsupial (*Potorus tridactylus*), and in hamster cell lines. Some PAs induce micronuclei formation in erythrocytes in the bone marrow and foetal liver in mice, sister chromatid exchanges in a Chinese hamster cell line and human lymphocytes *in vitro*, and repair DNA synthesis in rodent hepatocyte cell cultures. Chromosome aberrations have been reported in the blood cells of children suffering from veno-occlusive disease (VOD), presumably caused by fulvine.

A number of PAs have been shown to be mutagenic in the *Salmonella typhimurium* assay, after metabolic activation. The carcinogenic activity of PAs appears to parallel their mutagenic behaviour, but not their hepatotoxicity.

Heliotrine at doses of 50 mg/kg body weight or more, administered to rats during the second week of gestation, has been shown to induce several abnormalities in the foetus. Doses of 200 mg/kg body weight resulted in intrauterine deaths or resorption of foetuses. Dehydroheliotridine, the metabolic pyrrole derivative of heliotrine, was 2.5 times more effective on a molar basis than its parent PA in inducing teratogenic effects.

The ability of PAs to cross the placental barrier in the rat and to induce premature delivery or death of litters has been demonstrated. The embryo *in utero* appears to be more resistant to the toxic effects of PAs than the neonate. PAs are known to have passed through the mother's milk to the sucklings.

Megalocytosis, the presence of enlarged hepatocytes containing large, hyper-chromatic nuclei, is a characteristic feature of PA-induced chronic hepatotoxicity in experimental animals. The enlarged hepatocytes arise through the powerful antimitotic action of the pyrrole metabolites of PAs. This change has not been observed in the human liver, though human foetal liver cells *in vitro* culture become enlarged when exposed to PAs, indicating susceptibility to the antimitoxic effect of the alkaloids.

In experimental animals, protein-rich and sucrose-only diets have given some measure of protection against the effects of the alkaloids, as has pre-treatment of animals with thiols, anti-oxidants, or zinc chloride.

PAs are noted mainly for the poisoning of livestock due to the animals grazing on PA-containing toxic weeds, and large-scale outbreaks have been recorded. Such episodes have been reported from most parts of the world, including those with temperate or cold climates. Studies carried out on a wide variety of farm and laboratory animals have revealed generally common features of toxicity with some species variations. The liver is the principal target organ. In small laboratory animals, doses approaching a lethal dose produce a confluent, strictly zonal haemorrhagic necrosis in the liver lobule, within 12-48 h of administration of PAs. Simultaneously in non-human primates, or after a short time in the rat, chicken, and swine, changes begin to occur, and later become organized in their occlusion. The reticulin framework in the central zone of the lobule collapses following necrosis leading to scarring. Repeated administration of suitable doses leads to chronic liver lesions characterized by megalocytosis, and increasing fibrosis, which may result in cirrhosis. Chronic liver disease including cirrhosis has been shown to develop in the rat following administration of a single dose of a PA. In a number of animal species, the lungs develop vascular lesions characteristic of primary pulmonary hypertension with secondary hypertrophy of the right ventricle of the heart. In rats, appropriately low repeated doses of several alkaloids have been shown to induce tumours, mainly in the liver. In some studies, a single dose has been carcinogenic. The central nervous system is the target organ of the toxic PAs contained in *Trichodesma*, which produces spongy degeneration of the brain.

Effects on man

In man, PA poisoning is usually manifested as acute veno-occlusive disease characterized by a dull dragging ache in the right upper abdomen, rapidly filling ascites resulting in marked distension of the abdomen, and sometimes associated with oliguria, and massive pleural effusion. It can also manifest as subacute disease with vague symptoms and persistent hepatomegaly. Children are particularly vulnerable. Many cases progress to cirrhosis and, in some cases, a single episode of acute disease has been demonstrated to progress to cirrhosis, in spite of the fact that the

patient has been removed from the source of toxic exposure and has been given symptomatic treatment. Mortality can be high with death due to hepatic failure in the acute phase or due to haematemesis resulting from ruptured oesophageal varices caused by cirrhosis. Less severely affected cases may show clinical, or even apparently complete, recovery. The Task Group was not aware of any substantiated report of primary pulmonary hypertension resulting from PA toxicity. However, in view of the evidence in one case report, the possibility of the development of toxic pulmonary disease in man cannot be ruled out. There is a report of an outbreak of *Trichodesma* poisoning in the USSR in which the symptoms were mainly neurological.

Nature and extent of health risks

The two main sources of PA poisoning reported in human beings were the consumption of cereal grain contaminated by weeds containing the alkaloids and the use of alkaloid-containing herbs for medicinal and dietary purposes. A third form of exposure, with the potential to affect large populations is the possible low-level contamination of some foodstuffs, such as honey and milk, but the Task Group was not aware of any cases of human toxicity having been caused through the contamination of these foods.

Liver disease caused by the contamination of cereal grains has been reported in rural populations in Afghanistan, India, South Africa, and the USSR. A contributing factor appears to be abnormally dry weather, resulting in the growth of an exceptionally high proportion of the alkaloid-containing weeds in the crops, the seeds of which contaminate the cereal grain on harvesting. The weeds responsible for known oubreaks have been the *Heliotropium, Trichodesma, Senecio,* and *Crotalaria* species. Mortality in such outbreaks has been reported to be high. In the largest reported outbreak in northwestern Afghanistan, an estimated 8000 people were affected in a total population of 35,000 with 1600-2000 deaths.

Human poisoning through the medicinal use of herbs containing PAs has been reported from all parts of the world. PAs were responsible for a common liver disease in children in Jamaica, and individual cases in Ecuador, Hong Kong, India, the United Kingdom, and the USA. The plants involved were species of *Crotolaria, Heliotropium, Senecio, Symphytum,* and *Gynura. Symphytum*-containing preparations present a particular hazard because of their widespread use and the generally high levels of individual exposures. The use of herbs is almost universal in traditional folk medicine and is increasing in developed countries. Some of the herbs used contain PAs and have a long-term toxicity that is unsuspected by the people taking them. Knowledge of the species used in herbal medicine and the frequency of such use is very limited in the scientific literature. About 40 such species are listed in this report, about one-third of which are in use in developed countries. They are often prescribed by herbalists, naturopaths, and other non-orthodox practitioners. The extent of the contribution to acute and chronic liver disease cannot be accurately assessed. It may also constitute an aetiological factor in cirrhosis of the liver and, once this stage is reached, it may not be possible to identify the cause as a PA.

PAs are known to be transmitted from the feed of dairy animals into milk and to cause toxic damage in the suckling young. One instance of large-scale contamination of honey is known to have been caused by a common weed rich in PAs, which was the source of nectar and pollen for the honey-secreting bees. No reports of cases of acute toxicity caused by consumption of contaminated dairy products or honey were available to the Task Group. Furthermore, no information is available on the possible presence of PAs or their metabolites in the meat of animals fed toxic weeds before slaughter; however, the possibility of toxic disease being caused through this medium is considered to be low.

There are no substantial, long-term follow-up data to assess whether exposure to PAs results in increased incidence of chronic liver disease or cancer in man. Available clinical and experimental data suggested that a single episode of PA toxicity and possibly also a long-term low level exposure may lead to cirrhosis of the liver. PAs could also be possible carcinogens in man, since a number of them have been demonstrated to induce cancer in experimental animals, the main target organ being the liver. These include some which have caused episodes of human toxicity, and some others which are found in herbs traditionally used as items of food. Also, in several instances of human toxicity, the reported daily rates of intake of such PAs were in close range of those known to induce tumours in rats. However, these risks cannot be adequately assessed on a quantitative basis. There are indications that PA intoxications leading to liver disease are more prevalent than the reported frequency of cases would seem to indicate.

Because of their known involvement in human poisoning and their possible carcinogenicity, exposure to pyrrolizidine alkaloids should be kept as low as practically achievable. The setting of regulatory tolerance levels for certain food products may be required in some situations.

Methods for prevention

The only known method of prevention is to avoid consumption of the alkaloids. In the USSR, a set of agricultural (or agrotechnical) legislative, phyto-sanitary and educational measures has prevented new outbreaks of poisoning due to *Heliotropium* and *Trichodesma,* since 1947.

Sources: 1. 'Environmental Health Criteria No. 80: Pyrrolizidine Alkaloids.' International Programme on Chemical Safety, World Health Organization, CH-1211, Geneva 27, Switzerland (1988).

2. 'Health and Safety Guide 26: Pyrrolizidine alkaloids.' International Programme on Chemical Safety, World Health Organization, CH-1211 Geneva 27, Switzerland (1989).

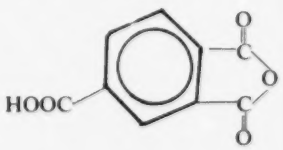
Trimellitic anhydride

The *IRPTC Bulletin* (Vol. 7 No. 1) reported in detail on trimellitic anhydride (TMA) and its toxicity to animals and man. It also set out the available scientific evidence on the biological impact of substances suspected of being harmful to man. It was also designed to contribute information to a wider scientific and public debate on the level of risk involved in exposure to such chemicals, on the acceptability of such risks and on the control measures that need to be adopted.

The Science and Technological Department of the Swedish National Chemicals Inspectorate has recently published

a report on trimellitic anhydride. The report is one in a series and was compiled according to the Organization for Economic Co-operation and Development guidelines for preparing chemical reviews. Its purpose is primarily to provide a basis for a hazard analysis of TMA. A hazard analysis is the first step in the process for decision-making applied by the Swedish National Chemicals Inspectorate. An analysis is devoted solely to an assessment of the inherent properties of a chemical substance and its capacity to harm man and environment. A subsequent risk assessment is the next step in the decision-making process and is not included in the hazard analysis report.

Identity

Common name:	Trimellitic anhydride
Chemical names: CAS:	5-isobensofurancarboxylic acid, 1,3-dihydro-1,3-dioxo
Synonyms and trade names:	Anhydro trimellitic acid; 1,2,4-benzenetricarboxylic acid anhydride; 1,2,4-benzenetricarboxylic acid, cyclic 1,2-anhydride; 1,2,4-benzenetricarboxylic anhydride; 4-carboxyphthalic anhydride; 1,3-dihydro-1,3-dioxo-5-isobenzofurancarboxylic acid; 1,3-dioxo-5-phthalancarboxylic acid; diphenylmethane-4,4'-diisocyanate-trimellic anhydride-ethomid HT polymer; NCI-C56633; 5-phthalanacarboxylic acid, 1,3-dioxo-; TMA; TMAN; trimellic acid anhydride; trimellic acid 1,2-anhydride; trimellitic acid cyclic 1,2-anhydride; trimellitic anhydride
Chemical structure:	
Molecular formula:	$C_9H_4O_5$
Registry numbers: CAS	552-30-7
RTECS	DC 2050000

Properties, production and use

Trimellitic anhydride is a white crystalline solid with a melting point of 161-163.5 °C and a boiling point of 240-245 °C. It is soluble in many solvents such as carbon tetrachloride, ligroin, mixed xylenes, dimethylformamide, acetone, and ethyl acetate.

TMA is produced mainly by subliming trimellitic acid above its melting point and also by heating crude trimellitic acid with V_2O_5. It is mainly used in the preparation of resins, adhesives, polymers, dyes and printing inks.

The anhydride group of the TMA is very reactive. It will hydrolyse in aqueous environments to trimellitic acid, but will react more readily with free amino groups on proteins to form conjugates. Consequently, it can act as a hapten in immunological reactions.

Effects on experimental animals

The available information is inadequate to properly assess the toxicokinetics of TMA. The acute oral and dermal toxicity of TMA in laboratory animals is low as is the toxicity produced by repeated oral administration for two weeks. The maximum tolerated oral dose of TMA to mice is slightly less than 625 mg/kg/day.

The anhydride is corrosive to the rabbit eye, and there is some indication that TMA is a skin irritant in rats and a skin sensitizer in guinea pigs. Results from a developmental toxicity screening test in mice do not indicate that TMA would pose a hazard to reproduction. However, this short-term *in vivo* assay is not adequate for the assessment of TMA as a substance which interferes with developmental stages in humans.

Two-week inhalation toxicity studies with TMA in rats have been shown to cause a dose-related increase in lung weight, external haemorrhagic lung foci, alveolar capillary haemorrhage, pneumonitis, and increases in TMA-specific serum and bronchoalveolar lavage fluid antibody levels.

Inhalation exposure to TMA in laboratory animals causes a sensitization which may produce both systemic and local antibody reactions. The anhydride mainly affects the lungs producing focal haemorrhages after prior sensitization has taken place. The immune response to inhaled TMA occurs in parallel with the development of lung lesions.

A rise in antibody levels (mainly IgE, IgA and IgM) in bronchoalveolar lavage and serum following inhalation of TMA are highly correlated with lung injury. Thus, these findings indicate that the antibody response in TMA sensitized animals plays a central role in the generation of lung lesions.

There are no data about chronic toxicity and carcinogenicity. Data on genotoxicity are inadequate; only negative results from *Salmonella* mutagenicity tests are available.

Effects on man

Exposure of humans to TMA in occupational environments mainly occurs by inhalation. Four clinical syndromes have been identified as being caused by inhalation of TMA dust or fumes. Three of these syndromes are associated with immunologically mediated respiratory tract reactions. The first is an immediate-type airway response characterized by asthma or rhinitis or both. These symptoms only occur when individuals are sensitized following a latent period of exposure from weeks to years. Once sensitization is acquired, symptoms occur within seconds or minutes of exposure. The syndrome is associated with a significant increase in total antibody activity and IgE to trimellityl-human-serum-albumin (TH-HSA) conjugates.

The second form, the late respiratory systemic syndrome (LRSS), also requires a latent period of exposure for sensitization. It is characterized by a late onset of symptoms such as coughing and wheezing which occur 4 to 12 hours after exposure to TMA; however, LRSS also includes arthralgias, myalgias and fever. This syndrome is often termed 'TMA-flu' and clinically resembles hypersensitivity pneumonitis. There are also high levels of IgG and IgA formed against TM-HSA.

The most severe reaction is the pulmonary disease-anaemia syndrome (PD-A) which may lead to respiratory failure. This illness is rare and has appeared only after exposures to high concentrations of TMA fumes, emanating from materials containing TMA, for relatively short periods. The symptoms vary in severity and may include haemoptysis, dyspnoea, pulmonary infiltrates, restrictive lung disease, hypoxaemia, and anaemia. The PD-A also requires a latent period of exposure before the onset of symptoms and it is characterized by high serum antibody levels. These symptoms are, however, reversible after withdrawal from TMA exposure.

The immunologic-based syndromes may depend on the high chemical reactivity of the anhydride which readily reacts with amino groups of proteins to form relatively stable hapten-protein-conjugates. Withdrawal of TMA exposure causes a decline both in antibody activity and clinical symptoms.

The fourth respiratory syndrome appears to be a non-immunologic irritant reaction to TMA. It is clinically characterized by a transient upper respiratory tract irritation with lacrimination and rhinorrhea and can occur in any worker after a significant exposure to TMA powder or fumes. However, this is not immunologically mediated and does not require a latent period of work exposure for the manifestation of symptoms. This reaction is provoked by the irritant effect of the anhydride and may also be of considerable clinical importance.

Conclusions

Inhalation exposure of animals with TMA has produced symptoms similar to LRSS and PD-A. As mentioned above, TMA-sensitized rats produced high concentrations of TMA-specific serum antibody in a dose-related manner. Histopathological examination of the lungs from TMA-treated rats resembled those obtained in human lung biopsies. The rats had high titers of TMA-specific serum antibody similar to the findings from TMA-exposed humans. Suppression of the immune system in rats has been shown to prevent TMA-induced lung lesions. Furthermore, passive sensitization of non-exposed rats to serum from TMA-sensitized rats was sufficient to induce TMA associated lung lesions by a single inhalation challenge. The production of TMA lung lesions, therefore, appears to be immunologically mediated. However, the immediate-onset-asthma which is characterized by serum IgE and asthmatic-type reactions has not been demonstrated in animal studies.

In conclusion, the available evidence shows that TMA dust or fumes is highly irritating to the eyes and respiratory system; the dust may cause corrosive eye damage, and frequent exposure can lead to respiratory sensitization with, in rare cases, quite severe symptoms.

Source: 'Trimellitic Anhydride (TMA).' Report No. 1/89. Swedish National Chemicals Inspectorate, P.O. Box 1384, S-171 27 Solna, Sweden (January 1989).

New Bone for Old

Bones and teeth may be strong, but they are not indestructible. Age, disease and injury take their toll, which is why scientists have been searching for some time for synthetic versions of these natural materials. A chemist at the University of Texas in Austin seems to have found a way of turning hydroxyapatite—the major component of bones and teeth—into useful products for surgeons and dentists.

This chemist has found ways to make hydroxyapatite (calcium hydroxyphosphate) in either a porous form, as a bone substitute, or in a harder dense form, as replacement tooth enamel. He said that the body recognizes the material as old bone, and therefore won't reject it.

In animal experiments, he and his co-workers have found that pieces of the porous material, when implanted into bones, slowly become resorbed by living bone cells. The bones become load bearing again in about six months, and 85% conversion of the implants to natural bone has been observed in rabbits after one to two years.

The denser form can be produced in moulded shapes for dental implants, or it can be plated onto the surface of teeth by passing 40V of electricity through them. Dental implants made of the porous material may also find a role as replacement roots that can be resorbed into the jaw in the same way the bone implants are. The dense material, as well as having promise for dental repair, could also be used to make artificial hip joints, or even entire bones in patients who have had cancerous bones removed.

The secret of this sucess lies in the way he makes the materials, which in the case of moulded implants involves high-temperature synthesis using phosphoric acid. The porus material is made by allowing the solvent to bubble out of the material as it hardens.

This material is not quite as well developed as Bioglass, another bioceramic material that can be used as a replacement for bone, though it may offer some advantages in terms of strength.

Source: Chemistry and Industry, 21 August 1989.

IV. General legislation on chemicals

Canada

Comparative examination of international legislation on chemical hazards

The Canadian Department of Justice published recently a document 'Protection Against Chemical Hazards: A Comparative Examination of the Laws of the United Kingdom, France, the Federal Republic of Germany, the European Economic Community, the United States of America, and Japan, and related Conventions and Activities of International Organizations'.

This comparative examination of the laws and regulations protecting the workers and the public against chemical hazards in the above-mentioned countries is based on interviews and documentation given by officials in government ministries/agencies responsible for chemical safety in the countries mentioned above, in the Environment Directorates of the European Economic Community (EEC) and the Organization for Economic Co-operation and Development (OECD), and in four international organizations—the International Labour Office (ILO), the International Register of Potentially Toxic Chemicals (IRPTC), the International Programme on Chemical Safety (IPCS), and the Food and Agriculture Organization of the United Nations (FAO).

The legislative competence and administrative regulations and practices have been described under five major headings: Management and control of toxic chemicals; Management and control of hazardous waste; Prevention of major industrial hazards; Protection of workers; and Enforcement mechanisms. A summary of the first two chapters was given in Bulletin Vol. 9 No. 2; the remaining three subjects are summarized below.

Prevention of major industrial hazards

This chapter describes the legal and administrative machinery for the prevention of and response to major industrial hazards, a subject which received fresh momentum after the unprecedented scale of harm caused by Union Carbide's pesticide plant in Bhopal, India. The chapter reviews the activities of international organizations, in particular those of the ILO which adopted a resolution in June 1985 concerning the promotion of measures against risks of accidents arising out of the use of dangerous substances and processes in industry. The deliberations of the Special Consultants of the ILO at their meeting in October 1985 are also very significant. The Special Consultants urged governments to ratify the Occupational Safety and Health Convention and to take certain urgently needed measures such as: (a) the establishment and implementation of a Control System based on identification, assessment, management of major accident prevention systems, and emergency operations; (b) the development of check-lists for use in the monitoring of standards in major hazard installations; and (c) the development of a comprehensive Manual of Major Hazard Control. The ILO Hazard Alert System is described in the chapter. The World Bank's 'Manual of Industrial Hazard Assessment techniques' is also referred to.

But the most important initiative in this area has come from the EEC which issued the 1982 Directive on Major Accident Hazards, better known as the Seveso Directive. The EEC was stimulated by serious accidents at Beek in Holland and Seveso and Manfredonia in Italy to prepare this Directive. The reports of the UK Advisory Committee on Major Hazards and the Consultative Document also appear to have been a factor influencing its preparation. The Directive covers both preventive actions and emergency responses. It sets out general requirements which apply to every industrial plant carrying out activities in which certain dangerous chemicals are processed or stored, and specific requirements which apply when certain dangerous substances in excess of the listed threshold quantities are or may be present. The Directive emphasizes prevention. If despite taking all preventive measures a major accident does occur, it prescribes the emergency measures that must be taken. This Directive has been implemented by three European countries: the UK through the Control of Industrial Major Accident Hazard Regulations of 1984; France, through a circular issued pursuant to the 1976 Law on Classified Installations; and the FRG, through the Twelfth Ordinance on the Implementation of BImSchG (subsequently modified).

The chapter highlights the recommendations of the UK Advisory Committee on Major Hazards, which was established by the Health and Safety Commission. The recommendations in the Second Report (1979) urge that the highest priority should be accorded to accident avoidance by inherently safe design, high reliability plant and learning from warning's or 'near misses' to make sure that lessons are learned and applied. The chapter also describes the French emergency preparedness plans, called 'plans ORSEC' (*organisation des secours*) and the recently introduced Emergency Measures Bill.

Finally, the chapter describes the USA measures introduced in October 1986, when Congress amended the provisions of the Comprehensive Environmental Response, Clean-Up and Liability Act to which the Emergency and Community Right-to-Know provisions were added under Title III. Unlike the European response, which emphasizes prevention, the United States approach has been *post hoc* emergency preparedness through well laid-out procedures involving the establishment of emergency organizations at the national, state and local government levels and coordinators at the industrial facility level. The community's 'Right-to-Know' is to be achieved through the information and reporting requirements, principally those provided by material Safety Data Sheets, Emergency and Hazardous Chemical Inventory data, etc., to which the public is given limited access. The philosophy appears to be that if the industry is forced to disclose the inventories of dangerous chemicals and the public is vigilant—assumptions quite unrealistic—enough pressure will be mounted on it to run

a safe operation. EPA officials also seem to believe that regular inspections are not an answer since governments do not have adequate resources to inspect every hazardous facility on a routine basis, that inspections cannot be thorough enough to detect every violation, that it would give a false sense of security to the public, and that it might even expose the Government to potential legal liability.

The United States Occupational Safety and Health Administration (OSHA) has, however, stepped up its preventive programme. Acting under statutory authority, its has recently issued the Hazard Communication Standard requiring employers to warn employees who are working with potentially dangerous chemicals of their danger, and the Safety and Health Guide of the Chemical Industry, containing Guidelines used by Compliance, Safety and Health Officers of OSHA to evaluate employer safety programmes, particularly in the areas of disaster prevention and emergency response. The chapter then makes a brief reference to recent legislation in New Jersey (e.g. the Major Hazardous Waste Facilities Act and Worker and Community Right-to-Know Act, both of 1983, and the Toxic Catastrophe Prevention Act of 1985), and in New York (e.g. the Hazardous Substances Bulk Storage Act 1984). The chapter concludes with a brief mention of the US Chemical Industry's emergency response system under programmes known as CAER (Community Awareness and Emergency Response), and NCRIC (National Chemical Response and Information Centre) which comprises a transportation emergency centre (CHEMTREC), a mutual network between shippers and carriers (CHEMNET), and an 800 telephone number for safety information, and a training programme for public emergency response units.

In none of the above programmes is any thought given to providing compensation to victims of disasters through an industry fund, or to punish operators of facilities for their negligence that creates risks or results in disasters. Workers in hazardous installations, and communities most vulnerable to them, can be protected by strengthening existing rights and by new clusters of human rights. For the workers, new labour laws embodying fundamental rights such as the right-to-know, the right of participation and co-determination, etc., referred to in the next chapter, can be enacted. For the communities, the rights would include a right and opportunity to participate in all decisions before a hazardous plant is permitted to locate in their midst, or allowed to be significantly modified, including the specification of safeguards to be demanded at the design and construction stage and during operation; a right to information about activities within the plant, including information on the nature and volume of hazardous chemicals in inventories; a right to independent community inspectors (in addition to government inspectors) to monitor activities with prior permission of the plant management; and a right of compensation through industry financed indemnity funds. Some of these rights can be secured through voluntary agreements between the community and the proponents of an industrial project (as in Japan) and some through legislation.

Penal laws can reinforce the protection of workers as well as the general public, by creating offences of negligent endangerment, whereby a failure to install or properly maintain apparatus or other devices, or to take precautions or safeguards against industrial accidents or disasters, would be punished severely, by imprisonment of responsible supervisors where death or serious bodily harm has followed or a serious risk thereof was created. Such laws can promote a 'safety culture' at all levels in an enterprise which is essential to the protection of life.

Protection of workers

In the fifth chapter the legal protection accorded to workers in the six jurisdictions, as well as the significant work done by the ILO, is described. The chapter begins with the basic philosophy underlying the legislation and programmes of these six jurisdictions and the ILO. It is succinctly stated in the UK Health and Safety at Work Act, that the employer must ensure, as far as is reasonably practicable, the health, safety and welfare at work of all his employees and every employee, while at work, must take reasonable care for the health and safety of himself and of those who may be affected by his acts and omissions at work, and cooperate with his employer to enable the latter to perform his duties and comply with the statutory provisions. The United States Occupational Safety and Health Act has the same basic philosophy: the employer must furnish 'employment and a place of employment which are free from recognized hazards' and employees must comply with occupational safety and health standards and all statutory provisions which are applicable to their own actions and conduct. It recognizes that the State has a primary responsibility to ensure workers' health and safety which cannot be avoided by leaving it entirely to agreements between the social partners. But unlike the UK Act, the USA Act places an overall responsibility for the protection of worker's health on OSHA, the State agency.

By contrast, the French and West German legislation places the responsibility for improving the conditions of health and safety of employees on Health, Safety and Working Committees and Works Councils, respectively, formed in every establishment employing over a certain number of workers, a shared responsibility under FRG law. This latter right of co-determination is in some measure introduced in the Japanese Industrial Safety and Health Law. The basic philosophy underlying the various conventions and recommendations of the ILO in the area of worker protection is essentially the same—prevention of diseases, the use of all practicable measures, the taking of appropriate measures to reduce exposure to harmful substances and the complete elimination of extremely hazardous substances. (See the description of the Occupational Cancer Convention and Recommendation, the Occupational Safety and Health Convention and the recent Asbestos Convention.)

The chapter then describes the various measures enshrined in the legislation and subordinate legal instruments of the various countries, that aim at achieving the policy goals. Five groups of measures are examined: (a) control of exposure, (b) medical measures (including monitoring and health surveillance), (c) technical measures, (d) rights accorded to workers e.g. information, instruction and training and (e) inspection and enforcement by State agencies.

Control of exposure to hazardous substances is the key health protection measure required by the legislation of all countries. To this end, the laws impose certain exposure limits, called 'control limits' in the UK, which are basically the Threshold Limit Values (TLVs) developed by the American Conference of Governmental Industrial

Hygienists (ACGIH) and prescribed in the USA and in the other countries (they are called MAK-values in the FRG). The UK has proposed new concepts to replace the TLVs: Maximum Exposure Limits (MELs) and Occupational Exposure Standards (OES). A MEL is the maximum permitted concentration of a listed substance within the breathing zone of a worker, averaged over a specified period. An OES is the maximum concentration of a listed substance within the breathing zone of a worker, averaged over a specified period, to which, according to current knowledge, nearly all workers may be exposed day after day without adverse health effect. The OES will replace the recommended limits and the MEL, the control limits. The MELs and OES are published as draft regulations, called the Control of Substances Hazardous to Health (COSHH) Regulations. The chapter also refers to the EEC Directives on exposure to certain substances, including the 1980 Framework Directive under which individual Directives have been issued. Health standards through control of exposure should be fully able to preserve workers' health. There cannot be compromises based upon cost-benefit and other economic criteria. The latter approach would hamper the fight against pollution in the workplace and its deleterious effect on workers' health.

It is, however, the way in which the exposure standards are developed that is crucial. In the USA, the TLVs are voluntary standards primarily developed by private bodies, such as ACGIH, in which there is very limited worker input. The USA is slowly replacing them by new standards developed by State agencies, and the National Institute for Occupational Safety and Health, acting through OSHA—with a measure of public involvement. In the FRG, the authority empowered to recommend maximum exposure levels is the Commission on Maximum Workplace Exposures, known as the MAK Commission, an independent, non-governmental scientific body which, through a special tri-partite body composed of government, industry and worker representatives, establishes TLVs—'technical guiding concentrations' or biological tolerance values for working materials. These TLVs are then prescribed by the government under the authority of the Dangerous Substances Ordinance (*Verordnung über gefährliche Stoffe*). In the UK and Japan a similar arrangement is in effect. The draft COSHH regulations were drafted by the Health and Safety Executive (HSE), which works under the direction of the Health and Safety Commission (HSC), both statutory bodies established by the Health and Safety at Work Act. The HSC is comprised of representatives of organizations of industries, employees, local governments and professional bodies, all of whom are appointed by the Minister of Labour after consultation. The Director-General and the two directors of the HSE are appointed by the HSC with the approval of the Minister. In drafting the COSHH regulations, the HSE was advised by the Advisory Committee on Toxic Chemicals, which has the same broad representation as the HSC. Similarly, in Japan an independent body, called the Central Labour Standards Council, is responsible for advising the Labour Minister on the development of exposure standards. The Council has representations of employers' and workers' organizations, experts and academics.

Medical measures, including monitoring and health surveillance, are an integral part of the worker protection system in all five countries. These are described in the chapter, with special emphasis on the proposals in UK's draft COSHH Regulations and Japan's Industrial Safety and Health Law. The purpose of periodic medical examination is to detect at the earliest stage symptoms of reaction to industrial pollutants so that preventive and curative measures can be taken promptly with respect to individual workers as well as with respect to the premises and work processes as a whole. Technical measures to prevent exposure are also key elements in worker protection. The chapter highlights the provisions of the Asbestos Convention especially those requiring States which ratify the Convention to ensure that adequate engineering controls and work practices and, where possible, alternative technology are adopted and adequate respiratory breathing equipment is provided as a supplementary, temporary emergency or exceptional measure and not as a substitute for technical control. The Convention also asks countries to take measures to prevent exposure to asbestos by replacing certain types by other materials or products. The ideas underlying the Asbestos Convention are very valuable and can be adapted for a whole range of dangerous substances in the workplace.

The responsibility for providing information about the substances in the workplace and the dangers posed by them, and for providing adequate instructions and training, is also a key feature of worker protection laws.

The chapter highlights the right of workers in the FRG under the Works Constitution Act, to complain to competent authorities on any operational matter which affects them. Workers can influence the work environment significantly, if they are given the right to information, full access to their own medical records, the right to participate in decision-making when health and safety matters are involved, the right to refuse dangerous work, the right to bring contraventions to the attention of public authorities responsible for worker health and safety, and the concomitant protection against discrimination, reprisals and loss of earnings. In this context, the chapter refers to the right given to a worker by the French Labour Code when it was amended in 1982, to refuse to work in a dangerous situation. The Code makes it illegal to discipline the worker in such circumstance. A right is also accorded to a worker in the USA by the OSHA Act, but it is a right to require OSHA inspectors to investigate imminent danger situations and, if they fail to do so, to obtain a mandamus from the court ordering OSHA to investigate. The worker is protected by the law against reprisals for asserting this right. The Industrial Safety and Health Law of Japan has also given a right (and protection against reprisal) similar to that given in the USA Act.

Enforcement mechanisms

The final chapter is concerned with the mechanisms used in the five countries to implement and enforce the laws described in the preceding chapters since a law is no better than its enforcement. It focuses on the administrative and civil remedies and criminal sanctions provided in the subject-matter legislation, as well as on criminal sanctions provided in the penal codes. The administrative remedies include 'improvement notices', 'prohibition notices', and 'notices to comply', seizure of substances, suspension and revocation of licences, orders to take remedial measures, and various administrative orders of the EPA and OSHA, e.g. prohibitory orders and 'stop sale, use, or removal'

orders, 'notices of violation', and 'citations', etc. Citizens suit provisions are a special feature of the USA laws. The chapter refers to the right of registered associations in France to join as civil parties before the penal jurisdictions to initiate a public proceeding for infractions. This right is granted in the Criminal Procedure Code and has also been expressly included in the Law on Waste Disposal and the Law on Classified Installation. The chapter also refers to the Japanese enforcement process which is 'low-key'. It employs administrative guidance and anti-pollution agreements in preference to the formal methods.

The final part of the chapter describes at length the criminal sanctions provided in the subject-matter legislation, and in the Criminal Codes, especially those of France and the FRG. The latter enacted in 1980 a special group of seven sections in the Strafgesetzbuch (StGB), under the title 'Crimes Against the Environment', transferring the criminal offence sections from BImSchG, WHG, AbfG and the Atomic Energy Act with some modification of definitions to cover more aspects and increases in punishment. ChemG has its own criminal sanctions since it was enacted after the StGB amendments. The criminal offences in the USA and Japanese health and environmental protection legislation, especially the rigorous sanctions of USA RCRA for knowing violations (fines of up to $1 million on corporations, $250,000 on individuals) are described at length. In practice, however, the fines imposed are small in all jurisdictions, including the USA, and prison sentences are rare, and, where imposed, seldom exceed one year. Like the FRG, Japan has a special law for the punishment of pollution-related offences. Although this law is not part of the Penal Code, the offenders are prosecuted by using the criminal procedure of the Penal Code. The Law for the Punishment of Crimes Relating to the Environmental Pollution which Adversely Affects the Health of Persons, which is the full title, provides for stiff fines (but not as dramatic as in the USA) and long jail sentences—up to seven years in extreme cases (the maximum under USA RCRA is fifteen years). Here too, like the USA, jail sentences are rare and, even when imposed, they seldom exceed one year. These rigorous sanctions have not impressed the courts which appear to be unsympathetic to public prosecutors demanding the full force of the law. A special feature of the Japanese law is its provision easing the burden on the prosecutor in proving causation, which is a serious obstacle in criminal as well as civil cases. Where a substance known to be dangerous has been discharged by an accused facility in such an amount as would in itself be sufficient to endanger life or health, and the substance has in fact endangered life or health, a presumption is created against the accused. This reverse onus in a criminal matter is likely to create legal and constitutional difficulties. It is, however, useful in civil actions and is in fact provided for in the Victims Compensation Law of Japan.

Further information and copies of this document are obtainable on request from Mr. Mohan A. Prabhu, Senior Counsel, Environmental Law, Department of Justice, Ottawa, Canada.

Source: Prabhu, Mohan A. *Protection Against Chemical Hazards: A Comparative Examination of the Laws of the United Kingdom, France, the Federal Republic of Germany, the European Economic Community, the United States of America, and Japan, and related Conventions and Activities of International Organizations.* Ottawa, Canada (January 1988).

European Economic Community

Export from and import into the Community of certain dangerous chemicals

On 16 June 1988, the Council of the European Communities published a Council Regulation (EEC No. 1734/88) concerning export from and import into the Community of certain dangerous chemicals. The Regulation has entered into force on 22 June 1989. The following is the Regulation as it has been published in the *Official Journal of the European Communities.*

'THE COUNCIL OF THE EUROPEAN COMMUNITIES,

Having regard to the Treaty establishing the European Economic Community, and in particular Article 130 S thereof,

Having regard to the proposal from the Commission,[1]

Having regard to the opinion of the European Parliament,[2]

Having regard to the opinion of the Economic and Social Committee,[3]

Whereas certain provisions of Community legislation, and in particular Directives 76/769/EEC, and 79/117/EEC, restrict the marketing and use of certain dangerous substances and preparations and prohibit the placing on the market and use of plant protection products containing certain active substances in the Member States of the Community; whereas these provisions do not apply to those products when they are intended for export to third countries;

Whereas international trade in certain chemicals which are banned or severely restricted in countries of export has caused international concern on grounds of protection of man and the environment;

Whereas measures are necessary for the protection of man and the environment, both in the Community and in third countries;

Whereas schemes for notification and information concerning international trade in such substances have been set up within the framework of international organizations, namely the Organization for Economic Cooperation and Development (OECD), the United Nations Environment Programme (UNEP) and the Food and Agriculture Organization (FAO);

Whereas the Community and its Member States have actively participated in the work of these and of other international organizations relating to banned and severely restricted substances; whereas it is appropriate that the Community acts upon the results of this work through uniform Community procedures;

Whereas the export of chemicals to which this Regulation applies should be made subjects to a common notification procedure which would permit the Community to notify third countries with regard to such exports;

Whereas it is necessary to ensure that the rules applicable within the Community for the packaging and labelling of banned or severely restricted chemicals should apply to such chemicals when destined for export;

Whereas it is necessary to inform all the Member States of notifications received from third countries with regard to import into the Community of substances banned or severely restricted under the legislation of those countries;

Whereas the common notification procedures should also provide a basis for an appropriate exchange of information within the Community, including information on the implementation of the international notification scheme;

Whereas to this end the Commission will report to the Council and to the European Parliament, before 1 January 1990 and thereafter every two years, in particular on any possible reaction from the country of destination; whereas on the basis of this report,

[1] OJ No. C 177, 15. 7. 1986, p. 5.

[2] OJ No. C 281, 19. 10 1987, p. 199.

[3] OJ No. C 232, 31. 8. 1987, p. 55.

and on a proposal from the Commission, the Council will consider, before 1 July 1990, the possibility of introducing into this Regulation the principle of prior informed choice;

Whereas the list of chemicals in Annex I should be subject to review at intervals and amendment as necessary; whereas any such amendment to Annex I should be made on the basis of proposals from the Commission and should be the subject of a decision by the Council by a qualified majority;

Whereas to facilitate the amendment to Annex II, a system should be set up providing for close collaboration between the Member States and the Commission by means of the Committee for the adaptation of that Annex to technical progress;

Whereas the Commission, in the light of the operation of this Regulation, may propose to the Council appropriate amendments thereto,

HAS ADOPTED THIS REGULATION:

Article 1: Objectives

The purposes of this Regulation is to establish a common system of notification and information for imports from and exports to third countries of certain chemicals which are banned or severely restricted on account of their effects on human health and the environment.

Article 2: Definition

For the purposes of this Regulation, the following definitions shall apply:

1. 'chemical subject to notification':
   the chemicals listed in Annex I, whether on their own or in preparations for which there is a labelling obligation;
2. 'export':
   (a) the permanent or temporary export of products meeting the conditions of Article 9 (2) of the Treaty;
   (b) the re-export of products not meeting the conditions referred to in (a) which are placed under a customs procedure other than transit procedures;
3. 'reference number':
   the number assigned by the Commission to each chemical when it is exported for the first time to a third country. This number remains unchanged for every subsequent export of the same chemical from the Community to the same third country.

Article 3: Designation of authorities

Each Member State shall designate the authority or authorities, hereafter referred to as the 'designated authority' or 'designated authorities', competent for the notification and information procedures laid down by this Regulation. It shall inform the Commission of such designation.

Article 4: Exports to third countries

1. When a chemical subject to notification is exported for the first time from the Community to a third country, the designated authority of the State, from which it is exported, shall take the necessary measures to ensure that the appropriate authorities of the country of destination receive notification of the fact. Such notification which shall as far as possible take place prior to export, must comply with the requirement set out in Annex II.

The designated authority shall send a copy of such notification to the Commission, which shall forward it to the designated authorities of the other Member States and to the International Register of Potentially Toxic Chemicals (IRPTC).

The Commission shall assign a reference number to each notification received and communicate it immediately to the designated authorities of the Member States. It shall periodically publish a list of these reference numbers in the *Official Journal of the European Communities*, stating the chemical concerned, and the third country of destination.

2. The designated authority of the relevant Member State shall inform the Commission as soon as possible of any significant reaction from the country of destination. The Commission shall ensure that the other Member States are informed as soon as possible of that country's reaction.

3. Every subsequent export of the chemical concerned from the Community to the same third country shall be accompanied by a reference to the number of the notification published in the *Official Journal of the European Communities* pursuant to the provisions of the third subparagraph of paragraph 1.

4. Notification must be given afresh, whenever major changes are made to the rules concerning the substances in question.

5. As regards the transmission of information within the meaning of paragraph 1, the Member States and the Commission shall take account of the need to protect the confidentiality of data and ownership, both in the Member States and in the countries of destination.

Article 5: Packaging and labelling

Any of the chemicals listed in Annex 1 which are intended for export shall be subject to such measures on packaging and labelling established in pursuance of Directive 67/548/EEC, as last amended by Directive 88/302/EEC, or as appropriate of other Directives covering dangerous preparations, as are applicable in the Member State from which the goods are to be exported or in which they have been produced. This obligation shall be without prejudice to any specific requirements of the importing country.

Article 6: Notification from third countries

1. Where the designated authority of a Member State receives a notification from the competent authority of a third country concerning the export to the Community of a chemical whose manufacture, use, handling, consumption, transport and/or sale is subject to prohibition or substantial legal restriction under that country's legislation, it shall send forthwith to the Commission a copy of that notification together with all relevant information.

2. The Commission shall forward forthwith to the Member States any notification received either directly or indirectly, together with all available information.

3. The Commission shall periodically evaluate the information received by the Member States and, if necessary, submit appropriate proposals to the Council.

Article 7: Exchange of information and monitoring

1. Member States shall regularly forward to the Commission information on the operation of the notification system provided for in this Regulation.

2. The Commission shall regularly compile a report on the basis of the information provided by the Member States and forward it to the Council and the European Parliament. This report shall consist, *inter alia*, of information on participation in international notification systems, on the cover provided by such systems and on how they are complied with by third countries.

3. As regards the information supplied pursuant to paragraphs 1 and 2, the Member States and the Commission shall take account of the need to protect the confidentiality of data ownership.

Article 8

If a Member State applies, with respect to substances other than those in Annex 1, a national system using similar information procedures in respect of third countries to those laid down in this Regulation, it shall inform the Commission, specifying the substances concerned.

The Commission shall forward this information to the Member States.

Article 9: Updating of Annexes

1. The list of chemicals in Annex I shall be reviewed by the Commission at intervals particularly in the light of experience gained in implementing this Regulation, with special regard to information received pursuant to Article 8, and on the basis of developments in Community rules and of developments within

the framework of the OECD, the UNEP and the FAO. It shall be amended as necessary by decisions taken by the Council by qualified majority on a proposal from the Commission.
2. The amendments required for adapting Annex II to scientific and technical progress shall be adopted in accordance with the procedure laid down in Article 21 of Council Directive 67/548/EEC.

Article 10

This Regulation shall enter into force 12 months after its publication in the *Official Journal of the European Communities*. This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Luxembourg, 16 June 1988.

ANNEX I

List of chemicals banned or severely restricted to certain uses owing to their effects on human health and the environment

Chemical	CAS number	EINECS number
1. Mercuric oxide	21908-53-2	2446547
2. Mercurous chloride (calomel)	10112-91-1	2333075
3. Other inorganic mercury compounds		
4. Alkyl mercury compounds		
5. Alkoxyalkyl and aryl mercury compounds		
6. Aldrin	309-00-2	2062158
7. Chlordane	57-74-9	2003490
8. Dieldrin	60-57-1	2004845
9. DDT	50-29-3	2000243
10. Endrin	72-20-8	2007757
11. HCH containing less than 99.0% of the gamma isomer	608-73-1	2101689
12. Heptachlor	76-44-8	2009623
13. Hexachlorobenzene	118-74-1	2042739
14. Camphechlor (toxaphene)	8001-35-2	2322833
15. Polychlorinated biphenyls (PCB), except mono- and dichlorinated biphenyls	1336-36-3	2156481
16. Polychlorinated terphenyls (PCT)	61788-33-8	2629682
17. Preparations with a PCB or PCT content higher than 0.01% by weight		
18. Tris (2,3 dibromopropyl) phosphate	126-72-7	2047999
19. Tris-aziridinyl-phosphinoxide	545-55-1	2088925
20. Polybrominated biphenyls (PBB)		
21. Crocidolite	12001-28-4	

CAS: Chemical Abstracts Service
EINECS: European Inventory of Existing Commercial Chemical Substances

ANNEX II

Information required pursuant to Article 4

1. Identity of the substance or preparation to be exported:

1.1. *Substances:*
- name in nomenclature of the International Union of Pure and Applied Chemistry,
- other names (usual name, trade name, abbreviation),
- CAS number (if available),
- main impurities of the substance, when particularly relevant.

1.2. *Preparations:*
- trade name or designation of the preparation,
- for each substance listed in Annex 1, percentage and details as specified under 1.1.

2. Information on precautions to be taken, including category of danger and risk, and safety advice.

3. The name, address, telephone and telex numbers of the designated authority from whom further information may be obtained.

4. Summary of regulatory restrictions and reasons for them.

5. Expected date of export.

6. Reference number, if known.

7. Country of export and country of destination.'

Source: Council Regulation (EEC) No. 1734/88 of 16 June 1988, concerning export from and import into the Community of certain dangerous chemicals. *Official Journal of the European Communities*, No. L 155/2 (22 June 1988).

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